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Description

TECHNICAL FIELD OF INVENTION

[0001] The present invention relates to new compounds and their use in medicine, particularly as agents able to treat and/or prevent infections caused by fungus.

BACKGROUND OF INVENTION

[0002] The discovery of penicillin ushered in the "antibiotic era" and the ability to cure infections which were previously often fatal.

[0003] The advantages offered by antibiotics in the treatment of infectious diseases are compromised due to the increase in the number of antibiotic-resistant bacterial strains. Antimicrobial resistance makes it difficult and more expensive to treat a variety of common infections, causing delays in effective treatment, or in worst cases, inability to provide appropriate therapy. The predictable consequences of resistance are increased morbidity, prolonged illness, a greater risk of complications, and higher mortality rates. The economic burden includes loss of productivity (loss in income, diminished worker productivity, time spent by family) and increased cost of diagnostics and treatment (consultation, infrastructure, screening, cost of equipment, drugs...). It has been reported that every year 25000 patients die in the European Union from a bacterial infection which is multiresistant to the presently existing drugs.

[0004] The problem of resistance also covers the major pathogenic fungi and yeasts, encompassing fungal infections, with ever increasing due to their behavior as typical opportunistic. To date, fungal infections continue to be an important cause of morbidity and mortality very high, and may reach up to 100% in some disseminated infections.

[0005] In addition, although already exists in the market more than 20 anti-HIV drugs, there is a need of new types of antiviral drugs to palliate the new resistances.

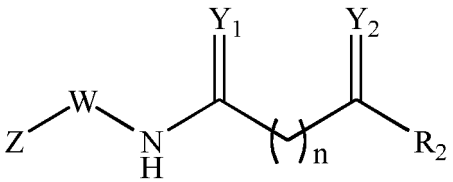
[0006] The requirements for new antibiotic, antifungal and antiviral molecules are in accordance with current problem of drug and multidrug resistance. It is an increasingly serious threat to global public health that drug resistance is present in all parts of the world. There are now very few effective drugs available to treat recently emerged multidrug resistant infections.

[0007] Fungicidal hydrazide compounds have been described in document DE2223936A1 as well as in documents accessible in the CAPLUS database under accession numbers 2010:489627 and 1949:30272. Justus Liebigs Annalen der Chemie 1897, 129-172 discloses hydroxy-oxalamic acid-(N'-phenyl-hydrazide).

[0008] There is still a need in the state of the art to identify suitable, effective new compounds for the prevention and/or treatment of infections.

SUMMARY OF THE INVENTION

[0009] In a first aspect, the invention relates to a compound of formula (I):

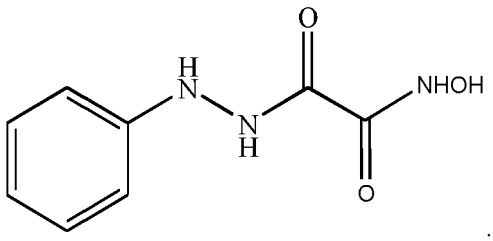


(I)

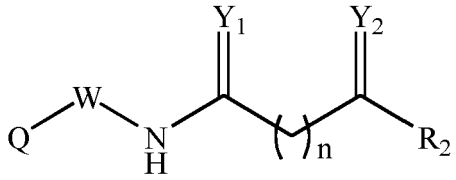
or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH;
n= 0, 1;
R_2= NHR_4, wherein R_4 is selected from the group consisting of, OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups;
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6}

alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl, aryl, -C(O)Rs, -OC(O)R_5, or -C(O)OR_5, wherein the term "alkyl" includes cyclic groups, with the proviso that when Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ and W is NH then Z is not a group selected from the group consisting of a pyridine group, and a phenyl group wherein the phenyl group is optionally substituted with methyl, halogen, NO_2 or OCH_3 group and with the proviso that the compound is not



[0010] In a second aspect, the invention relates to a compound of formula (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH;
n = 0, 1;
R_2= NHR_4, and wherein R_4 is selected from the group consisting of, OH, $-NH_2$, - NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups;
Q is selected from the group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, $-NH_2$, -NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)R_5-, -OC(O)R_5, or -C(O)OR_5,
c) 5-6 membered aromatic ring having one or more heteroatoms selected from the group consisting of N, S, and O and being optionally substituted with one or more groups independently selected from the group consisting of:

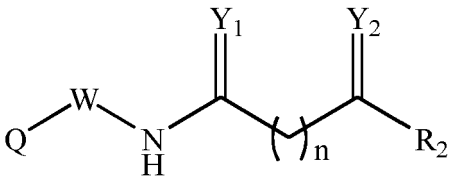
- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- NHC(O)R_5-, -C(O)NH-R_5, -OC(O)R_5, and -C(O)OR_5-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- OH, -SH or $-SR_5$ wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- $-NR_6R_7$, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,

wherein the term "alkyl" includes cyclic groups with the proviso that when $Y_1=Y_2=O$; n= 0; $R_2=NHNH_2$ and W is NH then Q is not a phenyl group,
or a pharmaceutical composition comprising said compound and a pharmaceutically acceptable excipient for use in medicine.

[0011] In a third aspect, the invention relates to a pharmaceutical composition comprising a compound of formula (II)



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH
n= 0, 1;
$R_2= NHR_4$, wherein R_4 is selected from, OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein
R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $- C(O)OR_5$, $- OC(O)R_5$, CF_3, CN, NH_2, -NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, wherein R_6 and R_7 are independently selected C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$-,.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- OH, -SH or -SR_5 wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, -$C(O)NH\text{-}R_5$, -$OC(O)R_5$, or -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

wherein the term "alkyl" includes cyclic groups and a pharmaceutically acceptable excipient for use in the prevention and/or treatment of an infection caused by fungus.

BRIEF DESCRIPTION OF THE FIGURES

[0012]

Figure 1. Antibiotic activities detected with the compounds MSG-210 (M-210), MSG-216 (M-216), MSG-196, (M-196) (Reference Example), MSG-214 (M-214), MSG-231 (M-231), MSG-235 (M-235). A: *T. pulmonis;* B: *N. cornea;* C: *S. pneumoniae;* D: *A. baumannii;* E: *T. pulmonis;* F: *N. cyriacigeorgica;* G: *E. faecalis;* H: *S. pneumoniae;* I: *A. baumannii.*

Figure 2. Antifungal activity of the compound MSG-119. Compound MSG-119 500 μg in *C.albicans* (A) and *A. terreus* (B); Compound 150 μg in *C. albicans* (C) and *A. terreus* (D). Control: Ketoconazole 50 μg, bottom spot of each figure.

Figure 3. Antifungal activity of the compound MSG-193. Compound 500 μg in *C.albicans* (A) and *A. niger* (B); Compound 150 μg in *C. albicans* (C) and *A. niger* (D). Control: Ketoconazole 50 μg, bottom spot of each figure.

Figure 4. Antifungal activity of the compound MSG-210. Compound 500 μg in *C.albicans* (A) and *A. niger* (B); Compound 150 μg in *C. albicans* (C) and *A. niger* (D) Control: Clotrimazole 10 μg bottom spot of each figure.

Figure 5. Antifungal activity of the compound MSG-214. Compound 500 μg in *C. lusitaniae* (A) and *A. niger* (B); Compound 150 μg in *C. lusitaniae* (C) and *A. niger* (D). Control: Clotrimazole 10 μg bottom spot of each figure.

Figure 6. Antifungal activity of the compound MSG-216. Compound 500 μg in *C. albicans* (A) and *C. lusitaniae* (B); Compound 150 μg in *C. albicans* (C) and *C. lusitaniae* (D). Control: Clotrimazole 10 μg bottom spot of each figure.

Figure 7. Antifungal activity of the compound MSG-218. Compound 500 μg in *C.albicans* (A) and *A. niger* (B); Compound 150 μg in *C. albicans* (C) and *A. niger* (D). Control: Clotrimazole 10 μg bottom spot of each figure.

Figure 8. Antifungal activity of the compound MSG-227. Compound 500 μg in *C. guillermondii* (A) and *A. terreus* (B); Compound 150 μg in *C. guillermondii* (C) and *A. terreus* (D). Control: Clotrimazole 10 μg bottom spot of each figure.

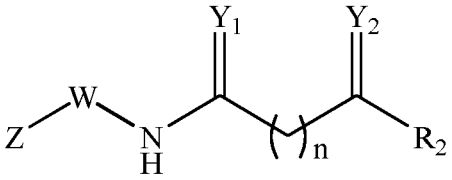
Figure 9. Anti-HIV activity of the compound MSG-119

DETAILED DESCRIPTION OF THE INVENTION

[0013] The inventors have identified new compounds having antibiotic, antifungal, and antiviral activity as shown in Examples 1-5.

Compounds of the invention

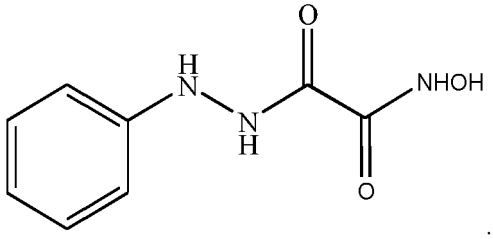
[0014] In a first aspect, the invention relates to a compound of formula (I):



(I)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O, ;
Y_2= O, ;
W= NH;
n= 0, 1;
R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, -NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups;
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, -NH_2, NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl, aryl, -C(O)Rs, -OC(O)R_5, or -C(O)OR_5, with the proviso that when Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ and W is NH then Z is not a group selected from the group consisting of a pyridine group, and a phenyl group wherein the phenyl group is optionally substituted with methyl, halogen, NO_2 or OCH_3 group and with the proviso that the compound is not



[0015] In a preferred embodiment of the compound of the invention is the compound of formula (I) wherein Y_1= O; Y_2= O; W= NH; n= 0, 1 and R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, -NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups and Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, - NH_2, NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl, aryl, -C(O)R_5, -OC(O)R_5, or -C(O)OR_5.

[0016] "Alkyl" refers to a straight or branched hydrocarbon chain radical consisting of carbon and hydrogen atoms, containing no unsaturation, and which is attached to the rest of the molecule by a single bond. Alkyl groups having 1, 2, 3, 4, 5, 6, or 7 carbon atoms are particularly preferred. Methyl, ethyl, n-propyl, iso-propyl and butyl, pentyl, hexyl, heptyl, including n-butyl, tert-butyl, sec-butyl and iso-butyl are particularly preferred alkyl groups. As used herein, the term alkyl, unless otherwise stated, refers to both cyclic and noncyclic groups, although cyclic groups will comprise at least three carbon ring members, such as cyclopropyl or cyclohexyl.

[0017] The term "C_{1-8} alkyl" refers to a linear or branched hydrocarbon chain radical consisting of carbon and hydrogen atoms, containing no insaturation, having between 1 and 8, preferably between 1 and 6 ("C_{1-6} alkyl"), carbon atoms and which is attached to the rest of the molecule by a single bond, including for example and in a non-limiting sense, methyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-pentyl, n-hexyl, t-hexyl, n-heptyl, t-heptyl, etc.

[0018] The term "C_{1-6} alkyl" refers to a linear or branched hydrocarbon chain radical consisting of carbon and hydrogen atoms, containing no insaturation, having between 1 and 6, preferably between 1 and 3 ("C_{1-3} alkyl"), carbon atoms and which is attached to the rest of the molecule by a single bond, including for example and in a non-limiting sense, methyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-pentyl, etc. Preferably "alkyl" refers to methyl or ethyl.

[0019] "Alkenyl" refers to a straight or branched hydrocarbon chain radical consisting of carbon and hydrogen atoms, containing one or more unsaturated bonds, and which is attached to the rest of the molecule by a single bond. The term "C_{1-8} alkenyl" refers to a linear or branched hydrocarbon chain radical consisting of carbon and hydrogen atoms, con-

taining one or more unsaturated bonds, having between 1 and 8 carbon atoms, preferably between 2 and 8 ("C_{2-8} alkenyl"), or more preferably between 2 and 6 ("C_{2-6} alkenyl") carbon atoms and which is attached to the rest of the molecule by a single bond. Examples of alkenyl groups include ethenyl, propenyl, allyl, butenyl, 1-methyl-2-buten-1-yl, and the like.

[0020] "Aryl" as used herein relates to single and multiple ring compounds, including multiple ring compounds that contain separate and/or fused aryl groups. Typical aryl groups contain from 1 to 3 separated and/or fused rings and from 6 to about 18 carbon ring atoms. In a particular embodiment the aryl group is a fused bicyclic aromatic ring wherein two aromatic rings are fused.

[0021] Preferably aryl groups contain from 6 to about 10 carbon ring atoms. Specially preferred aryl groups include phenyl, naphthyl, biphenyl, phenanthryl, anthracyl and the like. The term includes but is not limited to, phenyl, naphthyl, tetrahydronaphthyl, indanyl, indenyl, and the like. In a preferred embodiment the aryl is phenyl.

[0022] The term "C_{6-12} aryl" refers to an aromatic group having between 6 and 12, preferably between 6 and 10 ("C_{6-10} aryl"), more preferably 6 or 10 carbon atoms, comprising 1 or 2 aromatic nuclei, bound by means of a carbon-carbon bond or fused, including for example and in a non-limiting sense, phenyl, naphthyl, diphenyl, etc. Preferably "aryl" refers to phenyl.

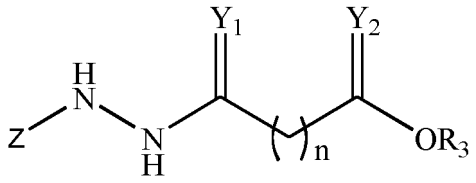
[0023] The term "aromatic heterocyclic ring" refers to an aromatic ring containing one or more heteroatoms in the structure. Preferably the heteroatom or heteroatoms in the aromatic heterocyclic ring are selected from N, S and O. Preferably, the aromatic heterocyclic ring is selected from 1-pyridine, 2-pyridine and 3-pyridine.

[0024] The terms "halogen", "halo" or "hal" refer to bromo, chloro, iodo or fluoro.

[0025] In a preferred embodiment, R_2 is NH-NH_2 or n is 1 and Y_1=Y_2= O. In another preferred embodiment, R_2 is NH-NH_2 and n is 1 and Y_1=Y_2= O.

[0026] In another preferred embodiment, Z is a phenyl group optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, -NH_2, NHOH, -$NHNH_2$, -NH-CH_3 and -NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, -OC(O)R_5, or -C(O)OR_5-.

[0027] Described herein but not part of the invention is compound of formula (III)

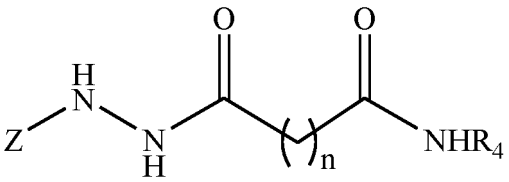


(III)

wherein

Y_1= O, NH;
Y_2= O, NH;
n= 0, 1;
R_3 is selected from H and C_1-C_6 alkyl, and
Z=1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -NO_2, C_{1-6} alkoxy, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, -CF_3, -CN, -NH_2, -NH-CH_3 and - NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen and wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)R_5,-NHC(O)R_5-, - C(O)NH-R_5, -OC(O)R_5, and -C(O)OR_5-.

[0028] In another preferred embodiment, the compound according to the invention is a compound of formula (IV)



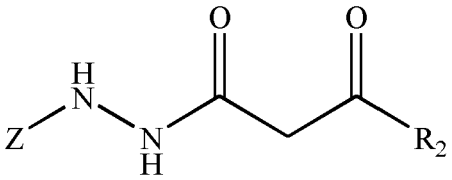
(IV)

wherein

n= 0, 1;
R_4 is selected from OH, and NH_2,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$, with the proviso that when $Y_1=Y_2=O$; n= 0 and R_4 is NH_2 then Z is not a group selected from a pyridine group, or a phenyl group optionally substituted with methyl, halogen, NO_2 and OCH_3 group and with the proviso that the compound is not the compound excluded from formula (I) above.

[0029] In another preferred embodiment, the compound according to the invention is the compound of formula (IV) wherein R_4 is NH_2.

[0030] In another preferred embodiment, the compound according to the invention is a compound of formula (V):



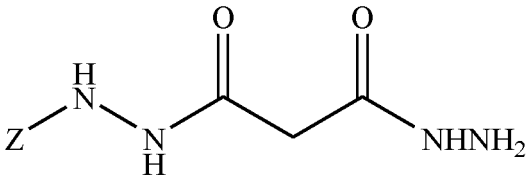
(V)

wherein

R_2= NHR_4, and wherein R_4 is selected from H, OH, C_1-C_6 alkyl, aryl groups, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or $-C(O)OR_5$.

[0031] In a preferred embodiment, the compound of the invention is a compound of formula (V) wherein R_2 is NHR_4, wherein R_4 is selected from OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups.

[0032] In a more preferred embodiment, the compound according to the invention is a compound of formula (VI):

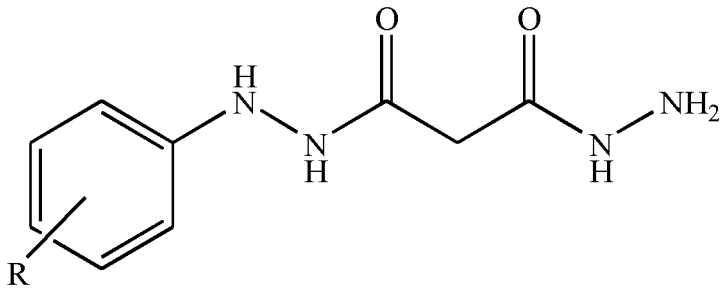


(VI)

wherein

Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$.

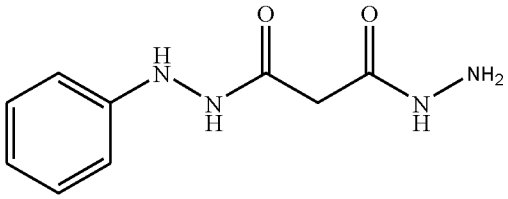
[0033] In another preferred embodiment, the compound according to the invention is a compound of formula (VII):



(VII)

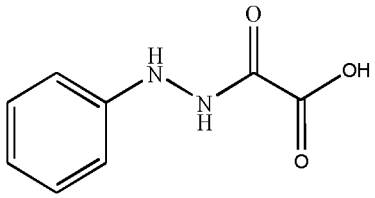
wherein the phenyl group is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or $-C(O)OR_5$.

[0034] In a more preferred embodiment, the compound of the invention is



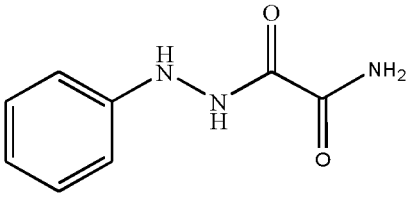
(Ia) MSG187.

[0035] Described herein but not part of the invention is



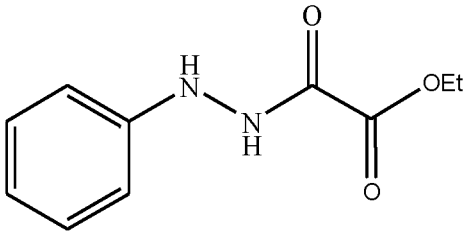
(Ic) MSG160.

[0036] In another preferred embodiment, the compound of the invention is



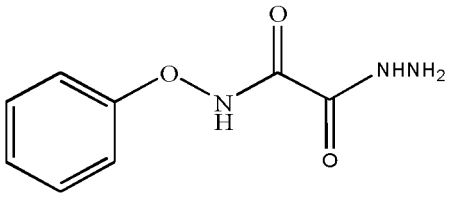
(Id) MSG159.

[0037] Described herein but not part of the invention is



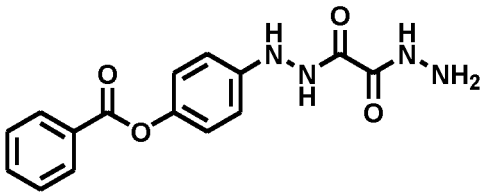
(Ie) MSG156.

[0038] Described herein but not part of the invention is



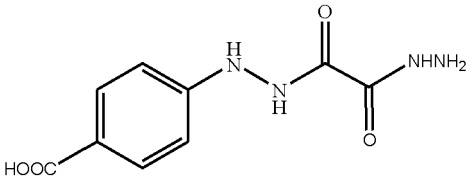
(If) MSG196.

[0039] In another preferred embodiment, the compound of the invention is



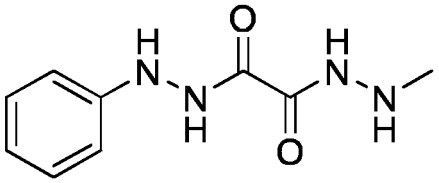
(Ig) MSG231.

[0040] In another preferred embodiment, the compound is:



(IIg) MSG223

or



(IIm) MSG161.

[0041] The invention also relates to a pharmaceutically acceptable salt, stereoisomer or solvate of a compound of the invention.

[0042] The term "salt" is to be understood as meaning any form of the active compound according to the invention in which this assumes an ionic form or is charged and is coupled with a counter-ion (a cation or anion) or is in solution. By this are also to be understood complexes of the active compound with other molecules and ions, in particular complexes which are complexed via ionic interactions. The definition includes in particular physiologically acceptable salts; this term must be understood as equivalent to "pharmacologically acceptable salts" or "pharmaceutically acceptable salts".

[0043] The term "physiologically acceptable salt" or "pharmaceutically acceptable salt" is understood in particular, in the context of this invention, as a salt (as defined above) formed either with a physiologically tolerated acid, that is to say salts of the particular active compound with inorganic or organic acids which are physiologically tolerated - especially if used on humans and/or mammals - or with at least one, preferably inorganic, cation which are physiologically tolerated - especially if used on humans and/or mammals.

[0044] For instance, pharmaceutically acceptable salts of compounds provided herein are synthesized from the parent compound, which contains a basic or acidic moiety, by conventional chemical methods. Generally, such salts are, for example, prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent or in a mixture of both. Generally, non-aqueous media like ether, ethyl acetate, ethanol, 2-propanol or acetonitrile are preferred. Examples of the acid addition salts include mineral acid addition salts such as, for example, hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, phosphate, and organic acid addition salts such as, for example, acetate, trifluoroacetate, maleate, fumarate, citrate, oxalate, succinate, tartrate, malate, mandelate, methanesulfonate and p-toluenesulfonate. Examples of the alkali addition salts include inorganic salts such as, for example, sodium, potassium, calcium and ammonium salts, and organic alkali salts such as, for example, ethylenediamine, ethanolamine, N,N-dialkylenethanolamine, triethanolamine and basic aminoacids salts. Since hydroxytyrosol has three hydroxyl groups, alkali addition salts are particularly preferred such as Na+ and NX4+ (wherein X is independently selected from H or a C1-C4 alkyl group).

[0045] Any compound referred to herein is intended to represent such specific compound as well as certain variations or forms. The compounds of the present invention represented by the above described formulas include stereoisomers.

The term "stereoisomer" as used herein includes any enantiomer, diastereomer or geometric isomer (E/Z) of such compound. In particular, compounds referred to herein may have asymmetric centres and therefore exist in different enantiomeric or diastereomeric forms. Thus any given compound referred to herein is intended to represent any one of a racemate, one or more enantiomeric forms, one or more diastereomeric forms, and mixtures thereof. Likewise, stereoisomerism or geometric isomerism related to a double bond is also possible, therefore in some cases the molecule could exist as (E)-isomer or (Z)-isomer (trans- and cis- isomers). If the molecule contains several double bonds, each double bond will have its own stereoisomerism, that could be the same or different than the stereoisomerism of the other double bonds of the molecule. All the stereoisomers including enantiomers, diastereoisomers and geometric isomers of the compounds referred to herein, and mixtures thereof, are considered within the scope of the present invention.

[0046] The compounds of the invention may be in crystalline form either as free compounds or as solvates (e.g. hydrates, alcoholates, particularly methanolates) and it is intended that both forms are within the scope of the present invention. Solvate may include water or non-aqueous solvents such as ethanol, isopropanol, DMSO, acetic acid, ethanolamine, and EtOAc. Solvates, wherein water is the solvent molecule incorporated into the crystal lattice, are typically referred to as "hydrates". Hydrates include stoichiometric hydrates as well as compositions containing variable amounts of water. Methods of solvation are generally known within the art.

[0047] When a disclosed compound is named or depicted by structure, it is to be understood that the compound, including solvates thereof, may exist in crystalline forms, non-crystalline forms or a mixture thereof. The compounds or solvates may also exhibit polymorphism (i.e. the capacity to occur in different crystalline forms). These different crystalline forms are typically known as "polymorphs". It is to be understood that when named or depicted by structure, the disclosed compounds and solvates (e.g., hydrates) also include all polymorphs thereof. Polymorphs have the same chemical composition but differ in packing, geometrical arrangement, and other descriptive properties of the crystalline solid state. Polymorphs, therefore, may have different physical properties such as shape, density, hardness, deformability, stability, and dissolution properties. Polymorphs typically exhibit different melting points, IR spectra, and X-ray powder diffraction patterns, which may be used for identification. One of ordinary skill in the art will appreciate that different polymorphs may be produced, for example, by changing or adjusting the conditions used in solidifying the compound. For example, changes in temperature, pressure, or solvent may result in different polymorphs. In addition, one polymorph may spontaneously convert to another polymorph under certain conditions.

[0048] Furthermore, any compound referred to herein may exist as tautomers. Specifically, the term tautomer refers to one of two or more structural isomers of a compound that exist in equilibrium and are readily converted from one isomeric form to another. Common tautomeric pairs are enamine-imine, amide-imidic acid, keto-enol, lactam-lactim, etc.

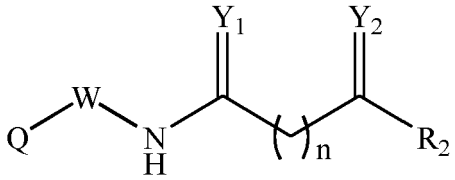
[0049] Unless otherwise stated, the compounds of the invention are also meant to include isotopically-labelled forms i.e. compounds which differ only in the presence of one or more isotopically-enriched atoms. For example, compounds having the present structures except for the replacement of at least one hydrogen atom by a deuterium or tritium, or the replacement of at least one carbon by ^{13}C- or ^{14}C-enriched carbon, or the replacement of at least one nitrogen by ^{15}N-enriched nitrogen are within the scope of this invention.

[0050] The compounds of the invention or their salts or solvates are preferably in pharmaceutically acceptable or substantially pure form. By pharmaceutically acceptable form is meant, inter alia, having a pharmaceutically acceptable level of purity excluding normal pharmaceutical additives such as diluents and carriers, and including no material considered toxic at normal dosage levels. Purity levels for the drug substance are preferably above 50%, more preferably above 70%, most preferably above 90%. In a preferred embodiment it is above 95% of the compound of the invention or of its pharmaceutically acceptable salt, stereoisomer or solvate.

[0051] A "metabolite" of a compound disclosed herein is a derivative of that compound that is formed when the compound is metabolized. The term "active metabolite" refers to a biologically active derivative of a compound that is formed when the compound is metabolized. The term "metabolized," as used herein, refers to the sum of the processes (including, but not limited to, hydrolysis reactions and reactions catalyzed by enzymes) by which a particular substance is changed by an organism. Thus, enzymes may produce specific structural alterations to a compound. For example, cytochrome P450 catalyzes a variety of oxidative and reductive reactions while uridine diphosphate glucuronyltransferases catalyze the transfer of an activated glucuronic-acid molecule to aromatic alcohols, aliphatic alcohols, carboxylic acids, amines and free sulphydryl groups.

[0052] The term "prodrug", as used herein, is intended to represent covalently bonded carriers, which are capable of releasing the compound of the inveniton as active ingredient when the prodrug is administered to a mammalian subject. Release of the active ingredient occurs *in vivo.* Prodrugs can be prepared by techniques known to one skilled in the art. These techniques generally modify appropriate functional groups in a given compound. These modified functional groups however regenerate original functional groups by routine manipulation or *in vivo.* Prodrugs of compounds of the invention include compounds wherein a hydroxy, amino, carboxylic, or a similar group is modified. Examples of prodrugs include, but are not limited to esters (e.g., acetate, formate, and benzoate derivatives), carbamates (e.g., N,N-dimethylaminocarbonyl) of hydroxy or amino functional groups in compounds of the invention), amides (e.g., trifluoroacetylamino, acetylamino, and the like), and the like.

[0053] In another aspect, the invention relates to a compound of formula (II)



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH
n= 0, 1;
R_2= NHR_4, wherein R_4 is selected from OH, $-NH_2$, - $NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, - $C(O)OR_5$, - $OC(O)R_5$, CF_3, CN, $-NH_2$, -NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

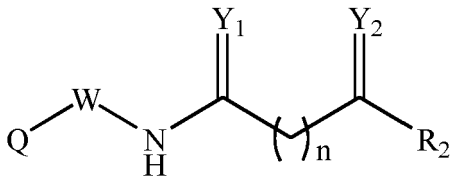
d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- OH, -SH or $-SR_5$ wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, or $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

wherein the term "alkyl" includes cyclic groups with the proviso that when Y_1= Y_2=O; n=0; R_2=$NHNH_2$ and W is NH, then Q is not a phenyl group or a pharmaceutical composition comprising said compound and a pharmaceutically acceptable excipient, for use in medicine.

Pharmaceutical composition of the invention

[0054] In a second aspect, the invention relates to a pharmaceutical composition comprising the compound of formula (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH
n= 0, 1;
R_2= NHR_4, wherein R_4 is selected from OH, -NH_2, - NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, - C(O)OR_5, - OC(O)R_5, CF_3, CN, -NH_2, -NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, -OC(O)R_5, or -C(O)OR_5-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, -C(O)NH-R_5, -OC(O)R_5, and -C(O)OR_5-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- OH, -SH or -SR_5 wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, -OC(O)R_5, or -C(O)OR_5, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, -C(O)NH-R_5, -OC(O)R_5, or -C(O)OR_5-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

wherein the term "alkyl" includes cyclic groups and a pharmaceutically acceptable excipient for use in the prevention and/or treatment of an infection caused by a fungus.

[0055] In a preferred embodiment, the pharmaceutical composition of the invention comprises the compound of formula (II) wherein Y_1= O; Y_2= O; W= NH; n= 0, 1; R_2= NHR_4, or aryl, and wherein R_4 is selected from OH, -NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups and Q is as previously described.

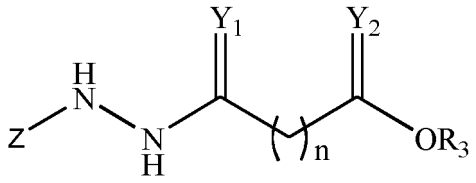
[0056] "Pharmaceutical composition" as used herein, relates to compositions and molecular entities that are physiologically tolerable and do not typically produce an allergic reaction or a similar unfavorable reaction as gastric disorders, dizziness and suchlike, when administered to a human or animal. Preferably, the term "pharmaceutically acceptable" means it is approved by a regulatory agency of a state or federal government or is included in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly in humans.

[0057] The term "excipient" refers to a vehicle, diluent or adjuvant that is administered with the active ingredient. Such pharmaceutical excipients can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and similars. Water or saline aqueous solutions and aqueous dextrose and glycerol solutions, particularly for injectable solutions, are preferably used as vehicles. Suitable pharmaceutical vehicles are described in "Remington's Pharmaceutical Sciences" by E.W. Martin, 21st Edition, 2005; or "Handbook of Pharmaceutical Excipients", Rowe C. R.; Paul J. S.; Marian E. Q., sixth Edition

[0058] Appropriate amounts of a compound of the invention as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof can be formulated with pharmaceutically acceptable excipients and/or carriers to obtain a pharmaceutical composition for use in medicine, particularly in preventing and/or treating an infection caused by a bacterium, fungi or virus.

[0059] Suitable pharmaceutically acceptable vehicles include, for example, water, salt solutions, alcohol, vegetable oils, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, surfactants, silicic acid, viscous paraffin, perfume oil, monoglycerides and diglycerides of fatty acids, fatty acid esters petroetrals, hydroxymethyl cellulose, polyvinylpyrrolidone and similars.

[0060] Described herein but not part of the invention is a compound according to the invention is a compound of formula (III)

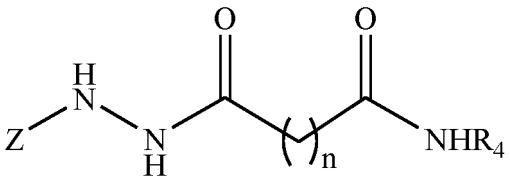


(III)

wherein

Y_1= O, NH;
Y_2= O, NH;
n= 0, 1;
R_3 is selected from H and C_1-C_6 alkyl, and
Z=1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -NO_2, C_{1-6} alkoxy, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, -CF_3, -CN, -NH_2, -NH-CH_3 and - NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen and wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)R_5,-NHC(O)R_5-, - C(O)NH-R_5, -OC(O)R_5, and -C(O)OR_5-.

[0061] In another preferred embodiment, the pharmaceutical composition of the invention comprises the compound according to the invention is a compound of formula (IV)



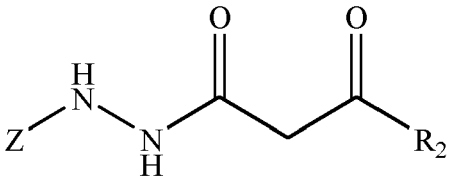
(IV)

wherein

n= 0, 1;
R_4 is selected from OH, and NH_2,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$,with the proviso that when $Y_1=Y_2=O$; n= 0; R_4 is NH_2 then Z is not a phenyl group and with the proviso that the compound is not the compound excluded from formula (I) above.

[0062] In a preferred embodiment, the pharmaceutical composition of the invention comprises a compound of formula (IV) wherein R_4 is NH_2.

[0063] Described herein but not part of the invention is a compound according to the formula (V)



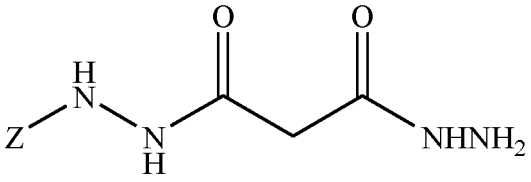
(V)

wherein

R_2= NHR_4, and wherein R_4 is selected from H, OH, C_1-C_6 alkyl, aryl groups, $-NH_2$, - $NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, - OR_5, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, - $OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, - NH_2NH_2, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, - $OC(O)R_5$, or $-C(O)OR_5$.

[0064] In a preferred embodiment, the pharmaceutical composition of the invention comprises a compound of formula (V) wherein R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups and Z is as previously described.

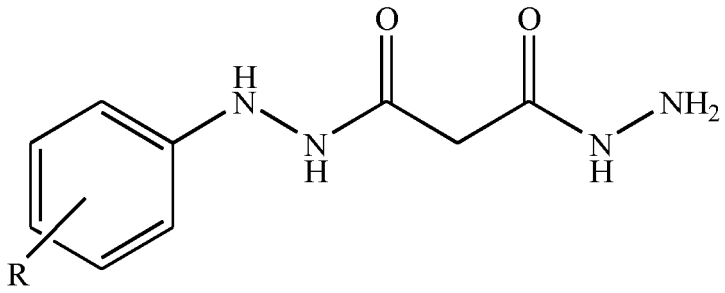
[0065] In a more preferred embodiment, the pharmaceutical composition of the invention comprises a compound of formula (VI):



(VI)

wherein
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, - $OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$.

[0066] In another preferred embodiment, the pharmaceutical composition of the invention comprises a compound of formula (VII):

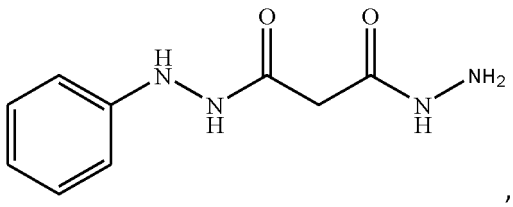


(VII)

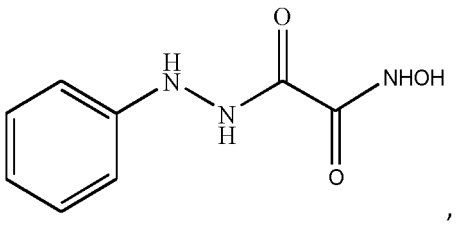
wherein the phenyl group is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or $-C(O)OR_5$.

[0067] In a preferred embodiment the pharmaceutical composition comprises a compound of formula (II) wherein $Y_1=Y_2=O$, n= 0, and Q is a phenyl group optionally substituted in para position with a group selected from the group consisting of H, halogen, CH_3 and OCH_3.

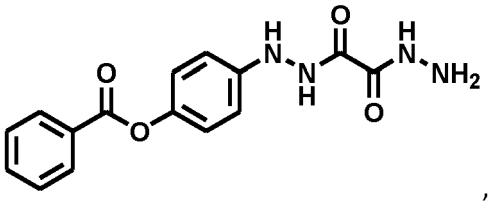
[0068] In a preferred embodiment the pharmaceutical composition comprises a compound selected from the group consisting of:



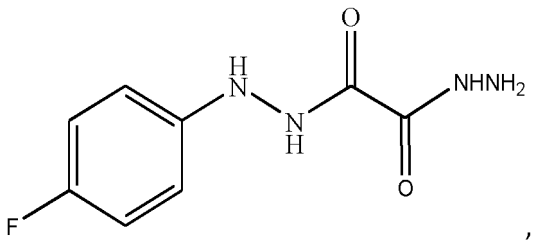
(Ia) MSG187



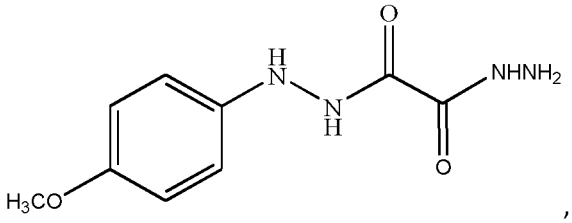
(Ib) MSG158



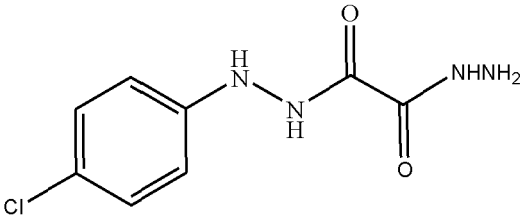
(Ig) MSG231

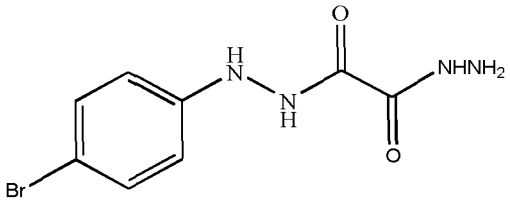


(IIb) MSG193

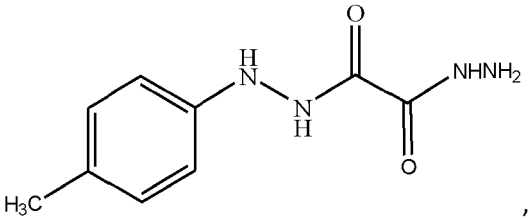


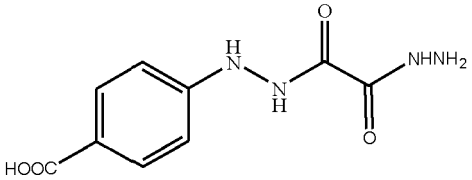
(IIc) MSG210



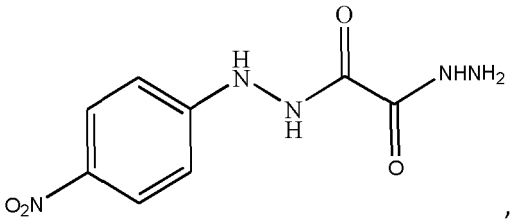


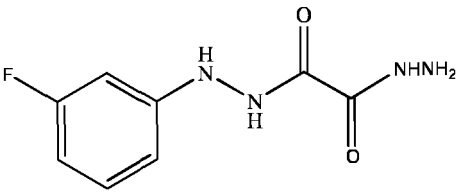
(IId) MSG214 (IIe) MSG216



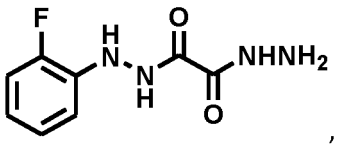


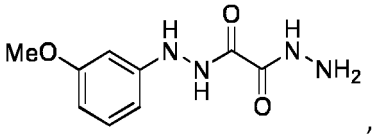
(IIf) MSG218 (IIg) MSG223



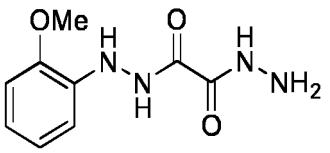


(IIh) MSG198 (IIi) MSG 227

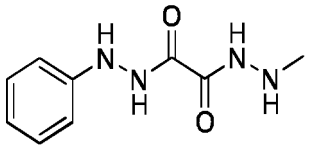




and (IIj) MSG235 (IIk) MSG 237



and



(III) MSG 239

(IIm) MSG161.

[0069] In a more preferred embodiment, the pharmaceutical composition comprises a compound selected from the group consisting of (Ia) MSG187, (Ib) MSG158, (Ig) MSG231, (IIb)MSG193, (IIc) MSG210, (IId) MSG214, (IIe) MSG216, (IIf) MSG218, (IIg) MSG223, (IIh) MSG198, (IIi) MSG 227 and (IIj) MSG235.

[0070] The pharmaceutical compositions containing the compound of the invention as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof according to the invention can occur at any pharmaceutical form of administration considered appropriate for the selected administration route, for example, by systemic (e.g intravenous, subcutaneous, intramuscular injection), oral, parenteral or topical administration, for which it will include the pharmaceutically acceptable excipients necessary for formulation of the desired method of administration. Additionally, it is also possible to administer the composition comprising the compound of the invention as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof of the invention intranasally or sublingually which allows systemic administration by a non-aggressive mode of administration. Also, intraventricular administration may be adequate. A preferred route of delivery is oral.

[0071] Those skilled in the art are familiar with the principles and procedures discussed in widely known.

[0072] Where necessary, the compound of the invention as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof is comprised in a composition also including a solubilizing agent and a local anesthetic to ameliorate any pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

[0073] In cases other than intravenous administration, the composition can contain minor amounts of wetting or emulsifying agents, or pH buffering agents. The composition can be a liquid solution, suspension, emulsion, gel, polymer, or sustained release formulation. The composition can be formulated with traditional binders and carriers, as would be known in the art. Formulations can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharide, cellulose, magnesium carbonate, etc., inert carriers having well established functionality in the manufacture of pharmaceuticals. Various delivery systems are known and can be used to administer a therapeutic of the present invention including encapsulation in liposomes, microparticles, microcapsules and the like.

[0074] Solid dosage forms for oral administration may include conventional capsules, sustained release capsules, conventional tablets, sustained-release tablets, chewable tablets, sublingual tablets, effervescent tablets, pills, suspensions, powders, granules and gels. At these solid dosage forms, the active compounds can be mixed with at least one inert excipient such as sucrose, lactose or starch. Such dosage forms can also comprise, as in normal practice, additional substances other than inert diluents, e.g. lubricating agents such as magnesium stearate. In the case of capsules, tablets, effervescent tablets and pills, the dosage forms may also comprise buffering agents. Tablets and pills can be prepared with enteric coatings.

[0075] Liquid dosage forms for oral administration may include emulsions, solutions, suspensions, syrups and elixirs pharmaceutically acceptable containing inert diluents commonly used in the technique, such as water. Those compositions may also comprise adjuvants such as wetting agents, emulsifying and suspending agents, and sweetening agents, flavoring and perfuming agents.

[0076] Injectable preparations, for example, aqueous or oleaginous suspensions, sterile injectable may be formulated according with the technique known using suitable dispersing agents, wetting agents and/or suspending agents. Among the acceptable vehicles and solvents that can be used are water, Ringer's solution and isotonic sodium chloride solution. Sterile oils are also conventionally used as solvents or suspending media.

[0077] For topical administration, compounds of the invention can be formulated as creams, gels, lotions, liquids, pomades, spray solutions, dispersions, solid bars, emulsions, microemulsions and similars which may be formulated according to conventional methods that use suitable excipients, such as, for example, emulsifiers, surfactants, thickening agents, coloring agents and combinations of two or more thereof.

[0078] Additionally, the compounds of the invention as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof may be administered in the form of transdermal patches or iontophoresis devices. In one

embodiment, the compounds of the invention are administered as a transdermal patch, for example, in the form of sustained-release transdermal patch. Suitable transdermal patches are known in the art.

[0079] Several drug delivery systems are known and can be used to administer the agents or compositions of the invention, including, for example, encapsulation in liposomes, microbubbles, emulsions, microparticles, microcapsules and similars. The required dosage can be administered as a single unit or in a sustained release form.

[0080] Sustainable-release forms and appropriate materials and methods for their preparation are described in, for example, "Modified-Release Drug Delivery Technology", Rathbone, M. J. Hadgraft, J. and Roberts, M. S. (eds.), Marcel Dekker, Inc., New York (2002), "Handbook of Pharmaceutical Controlled Release Technology", Wise, D. L. (ed.), Marcel Dekker, Inc. New York, (2000). In one embodiment of the invention, the orally administrable form of a compound according to the invention is in a sustained release form further comprises at least one coating or matrix. The coating or sustained release matrix include, without limitation, natural polymers, semisynthetic or synthetic water-insoluble, modified, waxes, fats, fatty alcohols, fatty acids, natural semisynthetic or synthetic plasticizers, or a combination of two or more of the them.

[0081] Enteric coatings may be applied using conventional processes known to experts in the art, as described in, for example, Johnson, J. L., "Pharmaceutical tablet coating", Coatings Technology Handbook (Second Edition), Satas, D. and Tracton, A. A. (eds), Marcel Dekker, Inc. New York, (2001), Carstensen, T., "Coating Tablets in Advanced Pharmaceutical Solids", Swarbrick, J. (ed.), Marcel Dekker, Inc. New York (2001), 455-468.

[0082] The present invention also encompasses the combination of the compounds of the invention or of its pharmaceutically acceptable salt, stereoisomer or solvate with other antimicrobial drugs. A combination of at least a compound of the invention and at least another antimicrobial drug may be formulated for its simultaneous, separate or sequential administration. This has the implication that the combination of the two compounds may be administered:

- as a combination that is being part of the same medicament formulation, the two compounds being then administered always simultaneously.
- as a combination of two units, each with one of the substances giving rise to the possibility of simultaneous, sequential or separate administration.

[0083] In a particular embodiment, the compound of the invention is independently administered from the other antimicrobial drug (i.e in two units) but at the same time.

[0084] In another particular embodiment, the compound of the invention is administered first, and then the other antimicrobial drug is separately or sequentially administered.

[0085] In yet another particular embodiment, the other antimicrobial drug is administered first, and then the compound of the invention is administered, separately or sequentially, as defined.

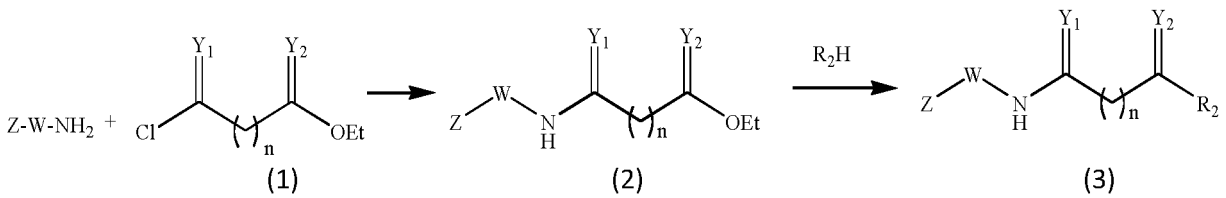
[0086] "Antimicrobial drug", as used herein, relates to any drug capable of killing bacteria, viruses, fungi or parasites or inhibit their growth. Antimicrobial medicines can be grouped according to the microorganisms they act primarily against, antibacterial, antifungal, antiviral and antiparasitic. In a preferred embodiment, the antimicrobial drug is an antifungal drug.

[0087] In additional preferred embodiments, the preferences described above for the different groups and substituents in the formulae above are combined. The present invention is also directed to such combinations.

[0088] All the terms and embodiments previously described are equally applicable to this aspect of the invention.

Process for obtaining the compounds of the invention

[0089] Compounds of formula (I) can be prepared through the following reactions (it has not been understood that the scope of the invention is defined by the appended claims and that the preparation of compounds not covered by the scope of the claims are intended for illustrative purposes only):



wherein

Y_1= O, NH;
Y_2= O, NH;
W= O, NH;

n= 0, 1;
R_2= OR_3 or NHR_4, wherein R_3 is selected from the group consisting of H, C_1-C_6 alkyl, and aryl; and wherein R_4 is selected from the group consisting of H, OH, C_1-C_6 alkyl, aryl groups, -NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups;
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, -NH_2, -NHOH, -NH-NH_2, -NH-CH_3 and - NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl, aryl, -C(O)Rs, -OC(O)R_5, or -C(O)OR_5, with the proviso that when Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ and W is NH, then Z is not a group selected from the group consisting of a pyridine group, and a phenyl group wherein the phenyl group is optionally substituted with methyl, halogen, NO_2 or OCH_3 group.

[0090] Preferably, the reactions are carried out in the presence of an organic solvent, such as a cyclic or acyclic ether (e.g. Et_2O, iPr_2O, tBu_2O, 1,4-dioxane, tetrahydrofuran, methyltetrahydrofuran), a hydrocarbonated solvent (e.g. pentane, hexane), a halogenated solvent (e.g. dichloromethane, chloroform), an alcohol (e.g. methanol, ethanol, propanol), an aromatic solvent (e.g. toluene, xylene), an amide (DMF, DMA) or mixtures thereof. In a particular embodiment, the reaction is performed in the presence of a halogenated solvent, such as dichloromethane.

[0091] A compound of formula (I) can preferably be prepared through reactions (1) and (2) in the presence of an organic solvent and the resulting compound is extracted in acid medium.

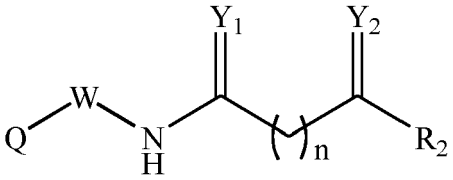
[0092] Preferably, the reaction is performed at a temperature between 0°C and room temperature, in the presence of an organic solvent

[0093] Preferably the method is for preparing a compound of formula (I) wherein Y_1= O;Y_2= O; W= NH; n= 0, 1; R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, -NH_2, -NH-CH_3 and -NRaRb, wherein Ra and Rb are independently selected C1-6 alkyl groups and Z is as previously described.

[0094] All the terms and embodiments previously described are equally applicable to this aspect of the invention.

Medical uses

[0095] In a second aspect, the invention relates to a compound of formula (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH;
n = 0, 1;
R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, -NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups;
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, -NH_2, -NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)R_5-, -OC(O)R_5, or -C(O)OR_5,
c) 5-6 membered aromatic ring having one or more heteroatoms selected from the group consisting of N, S, and O and being optionally substituted with one or more groups independently selected from the group consisting of:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- $-NR_aR_b$, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

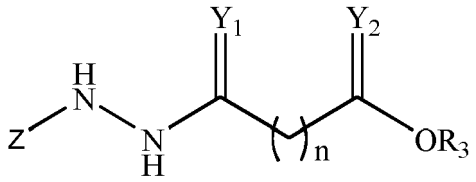
d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- OH, -SH or $-SR_5$ wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,

with the proviso that when Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ and W is NH then Q is not a phenyl group,
or a pharmaceutical composition comprising said compound and a pharmaceutically acceptable excipient for use in medicine.

[0096] In a preferred embodiment, the compound for use in medicine is the compound of formula (II) wherein Y_1= O; Y_2= O; W= NH; n = 0, 1; R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups; and Q is as previously described.

[0097] Described herein but not part of the invention is a compound of formula (III) for use in medicine

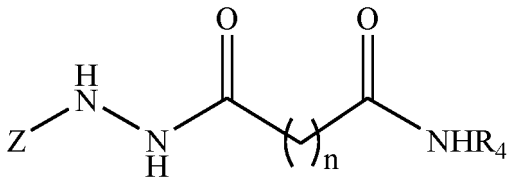


(III)

wherein

Y_1= O;
Y_2= O
n= 0, 1;
R_3 is selected from H and C_1-C_6 alkyl, and
Z=1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-NO_2$, C_{1-6} alkoxy, $C(O)NH-R_5$, $-C(O)OR_5$, - $OC(O)R_5$, $-CF_3$, -CN, $-NH_2$, $-NH-CH_3$ and - NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen and wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$,$-NHC(O)R_5$-, - $C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-.

[0098] In another preferred embodiment, the compound for use in medicine according to the invention is a compound of formula (IV)



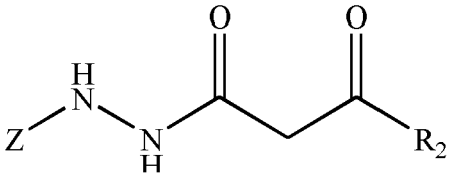
(IV)

wherein

n= 0, 1;
R_4 is selected from OH, and NH_2,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$,with the proviso that when $Y_1=Y_2=O$; n= 0 and R_4 is NH_2 then Z is not a phenyl group.

[0099] In a preferred embodiment, the compound for use in medicine is the compound of formula (IV) wherein R_4 is selected from OH and NH_2.

[0100] In another preferred embodiment, the compound for use in medicine according to the invention is a compound of formula (V):



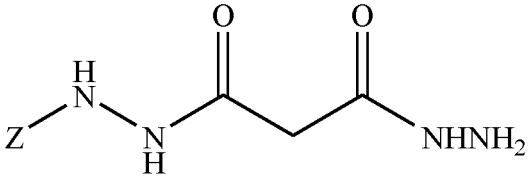
(V)

wherein

R_2= NHR_4, and wherein R_4 is selected from OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or $-C(O)OR_5$.

[0101] In a preferred embodiment, the compound for use in medicine is a compound of formula (V) wherein R_2= NHR_4, wherein R_4 is selected from OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups.

[0102] In a more preferred embodiment, the compound for use in medicine according to the invention is a compound of formula (VI):

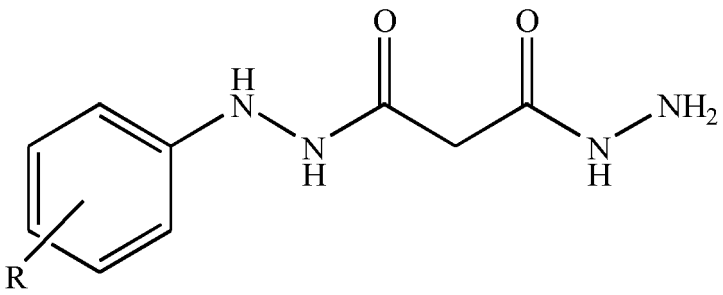


(VI)

wherein

Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, -NH-CH_3 and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)Rs$, $-OC(O)R_5$, or $-C(O)OR_5$.

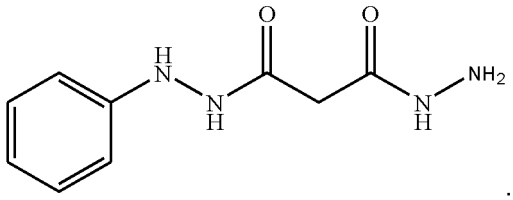
[0103] In another preferred embodiment, the compound for use in medicine according to the invention is a compound of formula (VII):



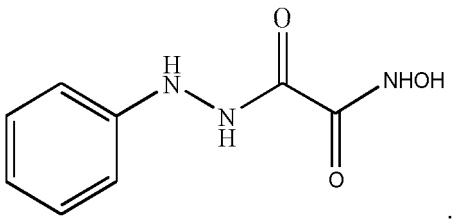
(VII)

wherein the phenyl group is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, -NH-CH_3 and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or $-C(O)OR_5$.

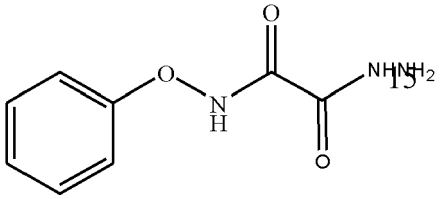
[0104] In a more preferred embodiment, the compound of the invention for use in medicine is selected with the exception of (If) MSG196 from the group consisting of:



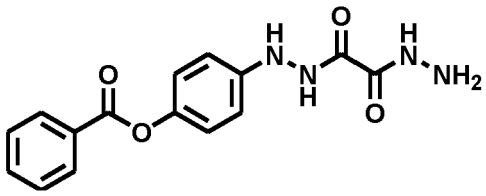
(Ia) MSG187



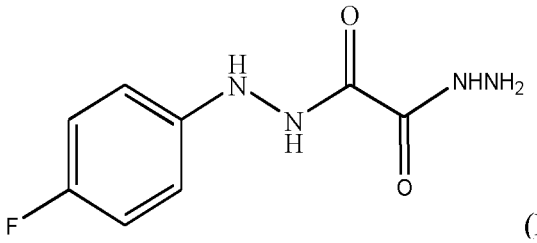
(Ib) MSG158



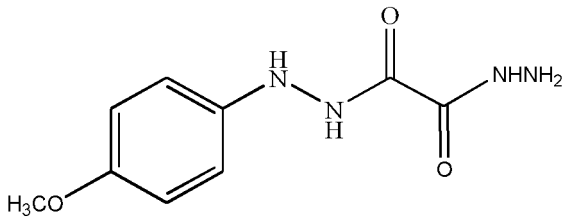
(If) MSG196 ,



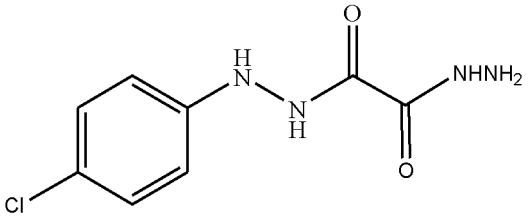
(Ig) MSG231



(IIb) MSG193,



(IIc) MSG210,



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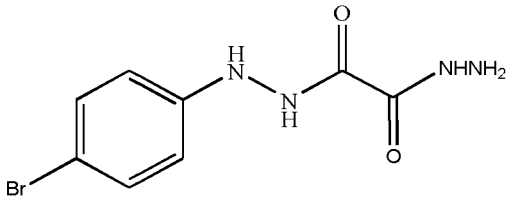

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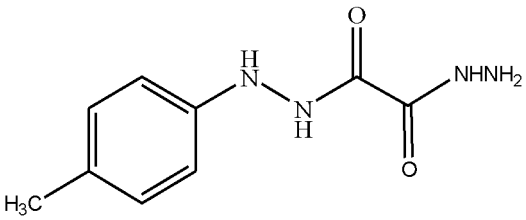
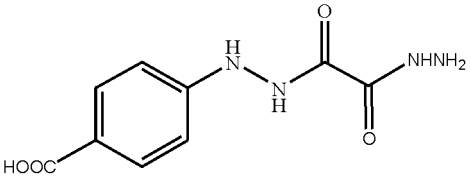
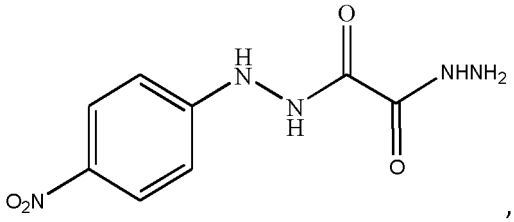
(IId) MSG214 (IIe) MSG216





(IIf) MSG218 , (IIg) MSG223



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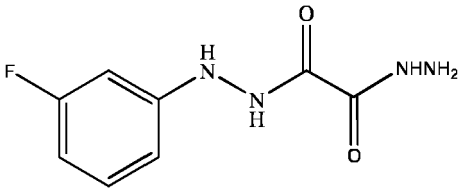
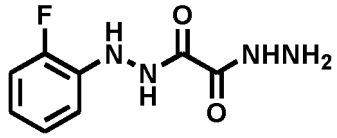


(IIh) MSG198 (IIi) MSG 227

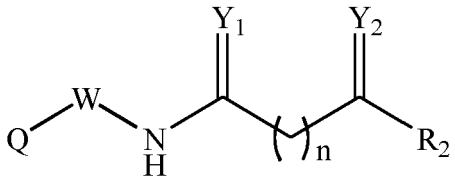
and



(IIj) MSG235.

[0105] In an even more preferred embodiment, the compound of the invention for use in medicine is selected from the group consisting of (Ia) MSG187, (Ib) MSG158, (Ig) MSG231, (IIb)MSG193, (IIc) MSG210, (IId) MSG214, (IIe) MSG216, (IIf) MSG218, (IIg) MSG223, (IIh) MSG198, (IIi) MSG 227 and (IIj) MSG235.

[0106] In a third aspect, the invention relates to a pharmaceutical composition comprising a compound of formula (II)



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O;
Y_2= O;
W= NH;
n= 0, 1;
R_2= NHR_4, wherein R_4 is selected from OH, C_1-C_6 alkyl, aryl groups, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, C(O)NH-R_5, - C(O)OR_5, -OC(O)R_5, CF_3, CN, NH_2, -NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_6 and R_7 are independently selected C_{1-6} alkyl groups, aryl groups, - C(O)Rs, -OC(O)R_5, or -C(O)OR_5-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, -C(O)NH-R_5, -OC(O)R_5, and -C(O)OR_5-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- (C_{1-6}alkyl)OCH_2-,

- C_{1-6} alkoxy,
- OH, -SH or -SR_5 wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, -$C(O)NH\text{-}R_5$, -$OC(O)R_5$, or -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

and a pharmaceutically acceptable excipient for use in the prevention and/or treatment of an infection caused by a fungus.

[0107] In another preferred embodiment, the pharmaceutical composition comprising a compound of formula (II), wherein Y_1= O, Y_2= O; W= NH, n= 0, 1; R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl group is for use in the prevention and/or treatment of an infection caused by a bacterium, fungus or virus. In another preferred embodiment, the pharmaceutical composition comprising a compound of formula (II), wherein Y_1= O, Y_2= O W= NH, n= 0, 1; R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl group is for use in the prevention and/or treatment of an infection caused by a fungus.

[0108] Also described but not forming part of the invention is a method for preventing and/or treating an infection caused by a bacterium, fungus or virus comprising administering a pharmaceutical composition comprising a compound of formula (II)

(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O, NH;
Y_2= O, NH;
W= O, NH
n= 0, 1;
R_2= OR_3 or NHR_4, wherein R_3 is selected from H , C_1-C_6 alkyl, and aryl, and wherein R_4 is selected from H, OH, C_1-C_6 alkyl, aryl groups, -NH_2, -NH-CH_3 and - NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, $C(O)NH\text{-}R_5$, - $C(O)OR_5$, -$OC(O)R_5$, CF_3, CN, NH_2, -NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_6 and R_7 are independently selected C_{1-6} alkyl groups, aryl groups, - C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, -$C(O)NH\text{-}R_5$, -$OC(O)R_5$, and -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

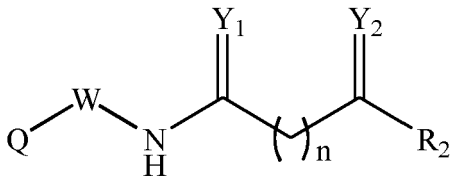
- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),

- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- OH, -SH or $-SR_5$ wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, or $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

to a subject in need thereof.

[0109] Also described but not forming part of the invention is a method which comprises administering a pharmaceutical composition comprising a compound of formula (II) wherein Y_1= O; Y_2= O;W= NH; n= 0, 1; R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl group. In another preferred embodiment, the method for preventing and/or treating an infection caused by a fungus, comprises administering a pharmaceutical composition comprising a compound of formula (II) wherein Y_1= O, Y_2= O W= NH, n= 0, 1; R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl group.

[0110] Also described but not forming part of the invention is a pharmaceutical composition comprising a compound of formula (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, wherein

Y_1= O, NH;
Y_2= O, NH;
W= O, NH
n= 0, 1;
R_2= OR_3 or NHR_4, wherein R_3 is selected from H , C_1-C_6 alkyl, and aryl, and wherein R_4 is selected from H, OH, C_1-C_6 alkyl, aryl groups, $-NH_2$, $-NH-CH_3$ and - NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, C(O)NH-R_5, - $C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, NH_2, -NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_6 and R_7 are independently selected C_{1-6} alkyl groups, aryl groups, - C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one

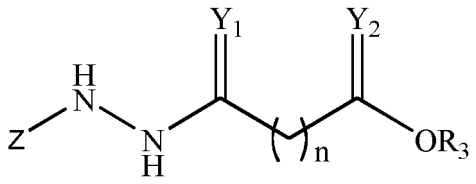
or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- $(C_{1-6}alkyl)OCH_2$-,
- C_{1-6} alkoxy,
- OH, -SH or -SR_5 wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, -$C(O)NH$-R_5, -$OC(O)R_5$, or -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

and a pharmaceutically acceptable excipient for the preparation of a medicament for preventing and/or treating an infection caused by a fungus.

[0111] The pharmaceutical composition for the preparation of a medicament for preventing and/or treating an infection caused by a fungus comprises a compound of formula (II) wherein Y_1= O; Y_2= O; W= NH; n= 0, 1; R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl group. In another preferred embodiment, the pharmaceutical composition for preventing and/or treating an infection caused by a fungus comprises a compound of formula (II) wherein Y_1= O, Y_2= O,, W= NH, n= 0, 1; R_2= NHR_4, wherein R_4 is selected from OH, - NH_2, -NH-CH_3 and -NR_aR_b, wherein R_a and R_b are independently selected C_{1-6} alkyl group.In a preferred embodiment Y_1=Y_2=O, n= 0, and Q is a phenyl group optionally substituted in para position with a group selected from the group consisting of H, halogen, CH_3 and OCH_3.

[0112] Described herein but not part of the invention is the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a bacterium, fungus or virus comprising a compound of formula (III)



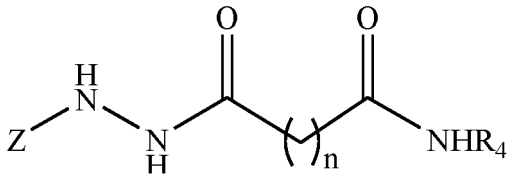
(III)

wherein

Y_1= O, NH;
Y_2= O, NH;
n= 0, 1;
R_3 is selected from H and C_1-C_6 alkyl, and
Z=1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -NO_2, C_{1-6} alkoxy, C(O)NH-R_5, -$C(O)OR_5$, -$OC(O)R_5$, -CF_3, -CN, -NH_2, -NH-CH_3 and - NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen and wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -$C(O)R_5$,-$NHC(O)R_5$-, - $C(O)NH$-R_5, -$OC(O)R_5$, and -$C(O)OR_5$-.

[0113] The pharmaceutical composition comprising a compound of formula (III) is for use in the prevention and/or treatment of an infection caused by a fungus.

[0114] In another preferred embodiment, the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a fungus comprises a compound of formula (IV)



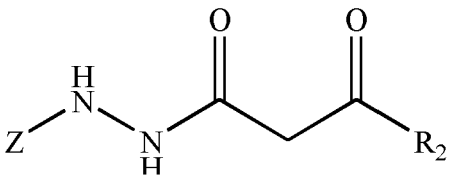
(IV)

wherein

n= 0, 1;
R_4 is selected from OH, and NH_2,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$.

[0115] In another preferred embodiment, the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a fungus comprises a compound of formula (IV) wherein R_4 is selected from OH, and NH_2..

[0116] In another preferred embodiment, the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a fungus comprises a compound of formula (V):



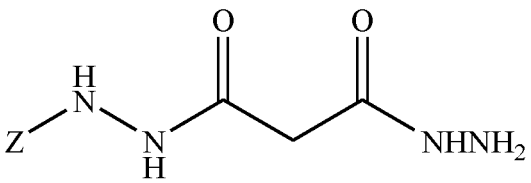
(V)

wherein

R_2= NHR_4, and wherein R_4 is selected from OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or $-C(O)OR_5$.

[0117] In a preferred embodiment, the pharmaceutical composition for use in the prevention of an infection caused by a fungus comprises a compound of formula (V) wherein R_2 is NHR_4, wherein R_4 is selected from OH, $-NH_2$ and $-NH-CH_3$. In another preferred embodiment, the pharmaceutical composition comprising a compound of formula (V) wherein R_2 is NHR_4, wherein R_4 is selected from OH, $-NH_2$ and $-NH-CH_3$ is for use in the prevention of an infection caused by a fungus.

[0118] In a more preferred embodiment, the the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a fungus comprises a compound of formula (VI):



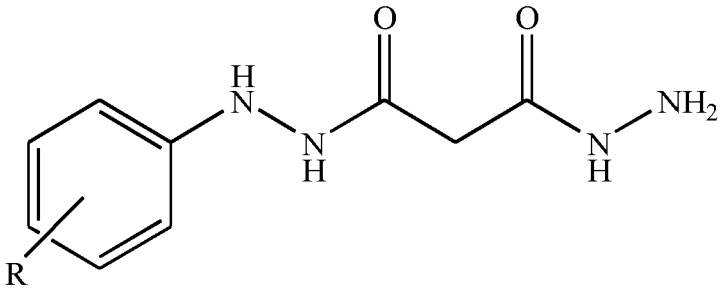
(VI)

wherein

Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, C(O)NH-R_5, $-C(O)OR_5$, - $OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$.

[0119] In a preferred embodiment, the pharmaceutical composition comprising a compound of formula (VI) is for use in the prevention and/or treatment of an infection caused by a fungus.

[0120] In another preferred embodiment, the the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a fungus comprises a compound of formula (VII):

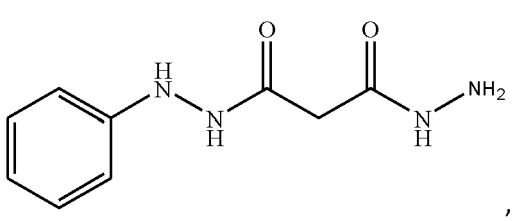


(VII)

wherein the phenyl group is optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, C(O)NH-R_5, $-C(O)OR_5$, - $OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH_2NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, $-C(O)R_5$, $-OC(O)R_5$, or - $C(O)OR_5$.

[0121] In a preferred embodiment, the pharmaceutical composition comprising a compound of formula (VII) is for use in the prevention and/or treatment of an infection caused by a fungus.

[0122] In another preferred embodiment of the medical uses, the compound is



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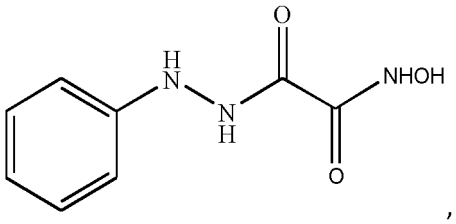

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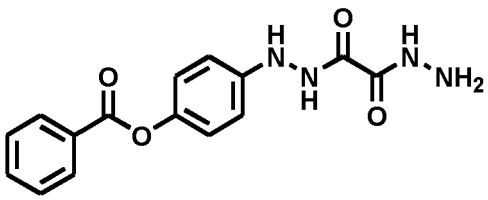
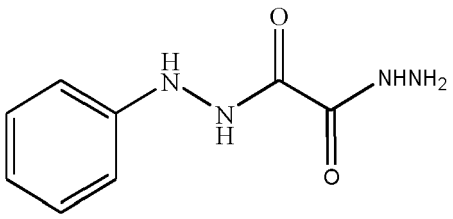
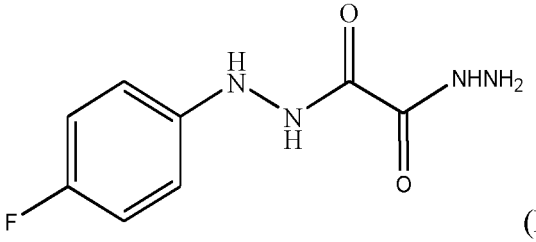
(Ia) MSG187 (Ib) MSG158



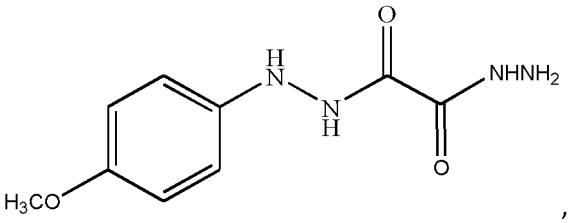
(Ig) MSG231



(IIa)MSG119 ,



(IIb) MSG193,



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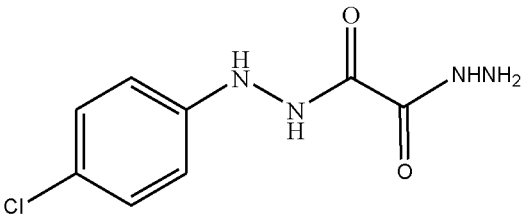
(IIc) MSG210



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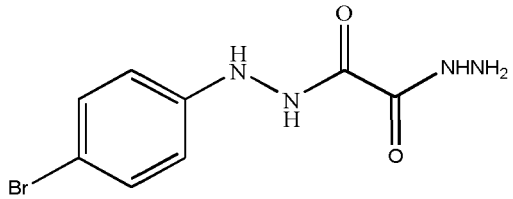

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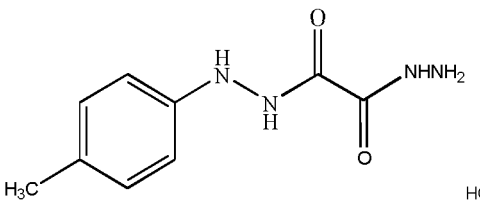
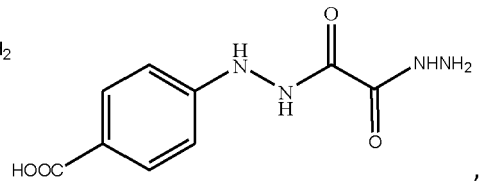
(IId) MSG214

(IIe) MSG216



(IIf) MSG218 ,



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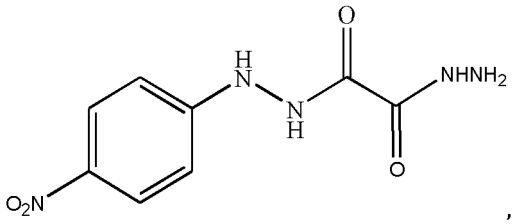
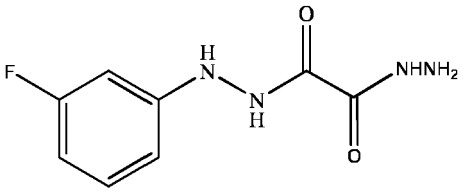
(IIg) MSG223

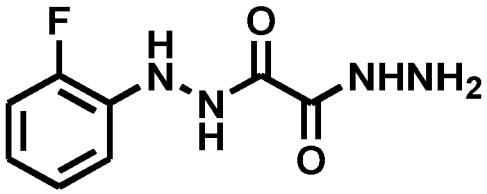


(IIh) MSG198 ,



(IIi) MSG 227

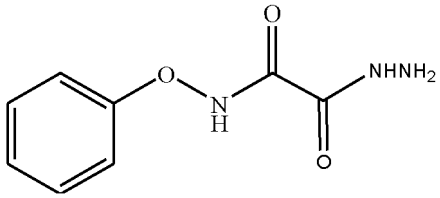
and



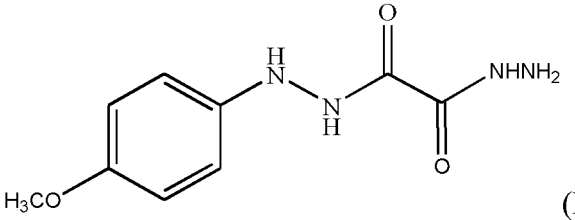
(IIj) MSG235

[0123] In a preferred embodiment of the medical uses of the invention, the pharmaceutical composition comprises a compound selected from the group consisting of (Ia) MSG187, (Ib) MSG158, (Ig) MSG231, (IIa)MSG119 , (IIb) MSG193, (IIc) MSG210, (IId) MSG214, (IIe) MSG216, (IIf) MSG218, (IIg) MSG223, (IIh) MSG198 (IIi) MSG 227 and (IIj) MSG235.

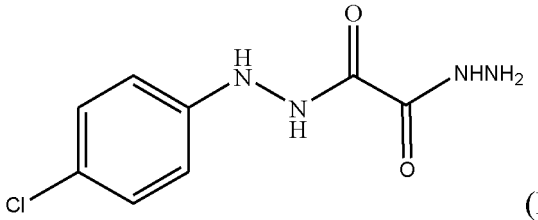
[0124] Described herein but not part of the invention is the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a bacterium comprises



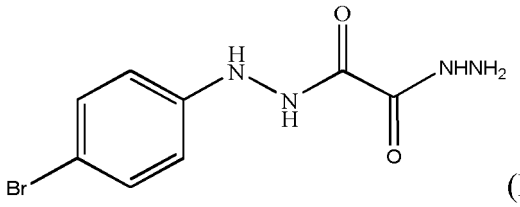
(If) MSG196,



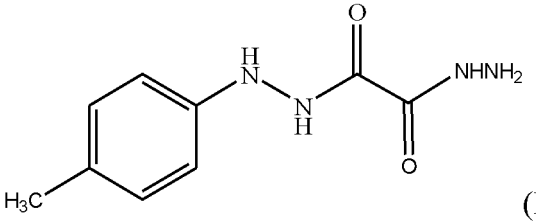
(IIc) MSG210,



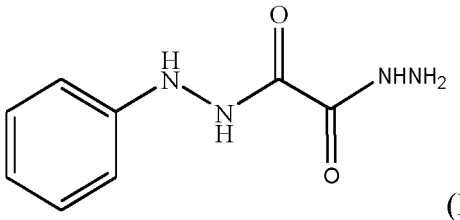
(IId) MSG214,



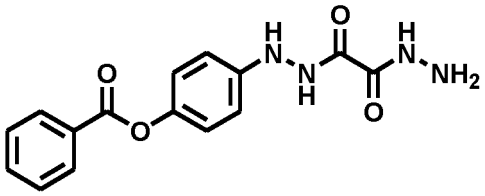
(IIe) MSG216 ,



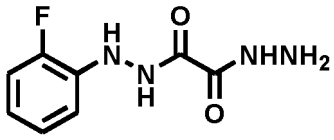
(IIf) MSG218 ,



(IIa) MSG119,

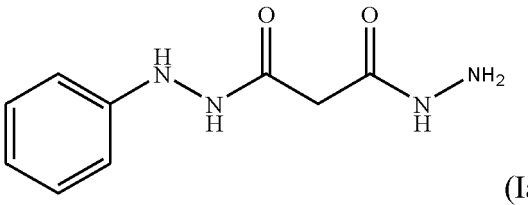


(Ig) MSG231 or

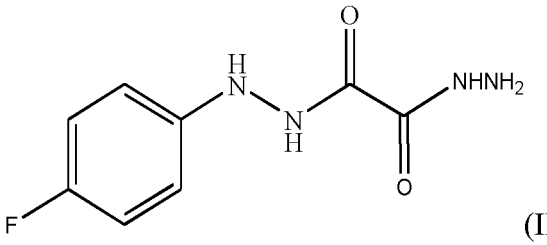


(IIj) MSG235.

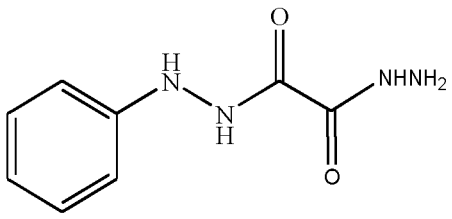
[0125] In another preferred embodiment, the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a fungi comprises



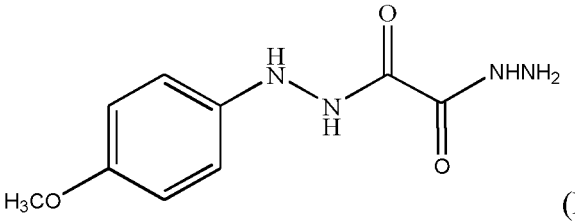
(Ia) MSG187,



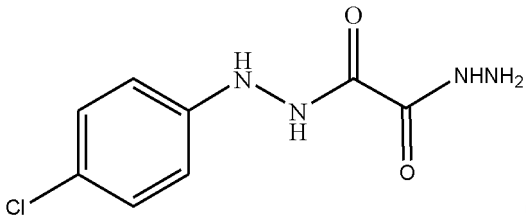
(IIb) MSG193,



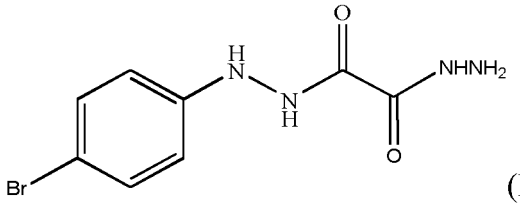
(IIa) MSG119 ,



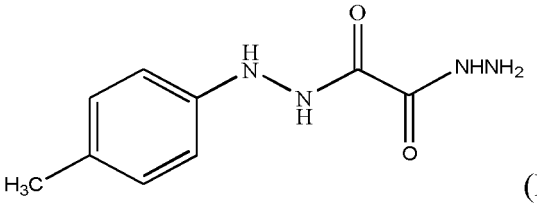
(IIc) MSG210,



(IId) MSG214,

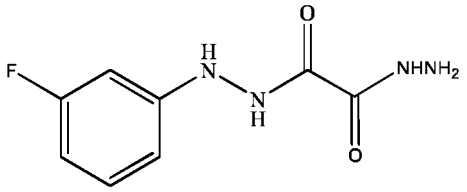


(IIe) MSG216 ,



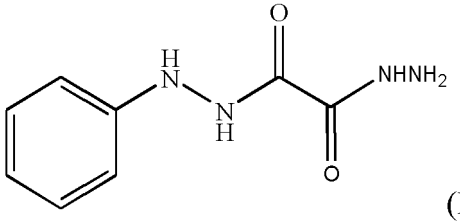
(IIf) MSG218 ,

or



(IIi) MSG 227.

[0126] In a more preferred embodiment, the pharmaceutical composition for use in the prevention and/or treatment of an infection caused by a virus comprises



(IIa)MSG119 .

[0127] As used herein, the terms "treat", "treating" and "treatment" include in general the eradication, removal, reversion, alleviation, modification, or control of the infection after its onset.

[0128] As used herein, the terms "prevention", "preventing", "preventive", "prevent" and "prophylaxis" refer to the capacity of a given substance, composition or medicament to avoid, minimize or difficult the onset or development of an infection before its onset.

[0129] The term "subject" as used herein, relates to any subject, particularly a mammalian subject, for whom therapy is desired. Mammalian subjects include humans, domestic animals, farm animals, and zoo, sports, or pet animals such as dogs, cats, guinea pigs, rabbits, rats, mice, horses, cattle, cows, and so on. In a preferred embodiment of the invention, the subject is a mammal. In a more preferred embodiment of the invention, the subject is a human.

[0130] The term "infection", as used herein, relates to invasion by bacteria, viruses, fungi, protozoa or other microorganisms, referring to the undesired proliferation or presence of invasion of pathogenic microbes in a host organism. It includes the excessive growth of microbes that are normally present in or on the body of a mammal or other organism. More generally, a microbial infection can be any situation in which the presence of a microbial population(s) is damaging to a host mammal. Thus, a microbial infection exists when excessive numbers of a microbial population are present in or on a mammal's body, or when the effects of the presence of a microbial population(s) is damaging the cells or other tissue of a mammal.

[0131] In a preferred embodiment, the infection is caused by a bacterium.

[0132] The term "bacterium" refers to both gram-negative and gram-positive bacterial cells capable of infecting and causing disease in a mammalian host, as well as producing infection-related symptoms in the infected host, such as fever or other signs of inflammation, intestinal symptoms, respiratory symptoms, dehydration, and the like.

[0133] In one embodiment the bacteria are gram-negative bacteria. In another embodiment the bacteria are gram-positive bacteria. In another further embodiment the bacteria are gram-positive bacteria together with gram-negative bacteria. In another embodiment there is only one bacteria specie or different bacteria species; one bacteria genus or different bacteria genus, infecting or causing disease.

[0134] In some embodiments, and without limitation, the bacteria is of a genus selected from the group consisting of *Acinetobacter, Actinobacillus, Aeromonas, Aggregatibacter, Agrobacterium, Bacillus, Bordetella, Brucella, Burkholderia, Campylobacter, Chromobacterium, Cyanobacteria, Enterobacter, Erwinia, Escherichia, Francisella, Fusobacterium, Haemophilus, Helicobacter, Klebsiella, Lactobacillus, Legionella, Listeria, Micrococcus, Moraxella, Mycobacterium, Neisseria, Nitrosomas, Nocardia, Obesumbacterium, Pantoea, Pasteurella, Pediococcus, Porphyromonas, Prevotella, Proteus, Pseudomonas, Ralstonia, Rhizobium, Rhodobacter, Salmonella, Serratia, Shigella, Staphylococcus, Streptococcus, Tannerella, Treponema, Tsukamurella, Vibrio, Xenorhabdus, Yersinia* and mixtures thereof. For example, in some embodiments and without limitation, the bacteria is of a species selected from the group consisting of *Aeromonas hydrophila, Aeromonas salmonicida, Acinetobacter baumannii, Aggregatibacter actinomycetemcomitans, Agrobacterium tumefaciens, Bacillus cereus, Bacillus subtilis, Burkholderia cepacia, Campylobacter jejuni, Chromobacterium violaceum, Enterobacter agglomeran, Erwinia carotovora, Erwinia chrysanthemi, Escherichia coli, Fusobacterium nucleatum, Haemophilus influenzae, Helicobacter pylori, Lactobacillus plantarum, Listeria monocytogenes, Klebsiella pneumoniae, Micrococcus luteus, Mycobacterium tuberculosis, Neisseria meningitidis, Neisseria gonorrhoeae, Nitrosomas europaea, Nocardia carnea, Obesumbacterium proteus, Pantoea stewartii, Pediococcus acidilactici, Prevotella interme-*

dia, Porphyromonas gingivalis, Pseudomonas aureofaciens, Pseudomonas aeruginosa, Pseudomonas phosphoreum, Pseudomonas syringae, Ralstonia solanacearum, Rhiszobium etli, Rhizobium leguminosarum, Rhodobacter sphaeroides, Salmonella typhimurium, Serratia liguefaciens, Serratia marcescens, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus enteritis, Tannerella forsythensis, Treponema denticola, Tsukamurella pulmonis, Vibrio anguillarum, Vibrio fischeri, Vibrio cholerae, Vibrio harveyi,, Vibrio parahaemolyticus, Vibrio alginolyticus, Vibrio vulnificus, Xenorhabdus nematophilus, Yersinia enterocolitica, Yersinia pestis, Yersinia pseudotuberculosis, Yersinia medievalis, Yersinia ruckeri and mixtures thereof.

[0135] In a preferred embodiment of the medical use of a compound of the inventionas defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, the infection is caused by a Gram positive bacterium.

[0136] In another preferred embodiment, the Gram positive bacterium is from phylum Actinobacteria or from phylum Firmicutes and/or the Gram negative bacterium is from phylum proteobacteria.

[0137] In a more preferred embodiment, the bacterium from phylum Firmicutes is a bacterium from genus *Staphylococcus, Bacillus* or *Enterococcus.* In a more preferred embodiment, the bacterium from genus *Staphylococcus* is *S. aureus or S. epidermidis,* the bacterium from genus *Bacillus* is *B. cereus* and the bacterium from genus *Enterococcus* is *E. faecium* or *E. faecalis.*

[0138] In a more preferred embodiment, the bacterium from phylum Actinobacteria is a bacterium from genus *Nocardia, Tsukamurella or Mycobacterium,* the bacterium from phylum Firmicutes is a bacterium from genus *Streptococcus, Clostridium* or *Enterococcus* and/or the bacterium from phylum proteobacteria is from genus *Acinetobacter, Pseudomonas, Klebsiella, Escherichia* or *Enterobacter.*

[0139] In an even more preferred embodiment, the bacterium from the genus Nocardia is *N. carnea* or *N.cyriacigeorgica,* the bacterium from genus *Tsukamurella* is *T. pulmonis,* the bacterium from genus *Mycobacterium* is *M. abscessus,* the bacterium from genus *Streptococcus* is *S. pneumoniae, S. epidermidis* or *S. pyogenes,* the bacterium from genus *Klebsiella* is *Kpneumoniae,* the bacterium from genus *Enterobacter* is *E. faecium, E. faecalis* or *E. cloacae,* the bacterium form genus *Escherichia* is *E. coli,* the bacterium from genus *Clostridium* is *C. difficile,* the bacterium from genus *Acinetobacter* is *A. baumannii* and/or the bacterium from genus *Pseudomonas* is *P. aeruginosa.*

[0140] In another preferred embodiment, the Gram negative bacterium is from phylum proteobacteria. In a more preferred embodiment, bacterium from phylum proteobacteria is from genus *Acinetobacter,* preferably *A. baumannii,* from genus *Pseudomonas,* preferably *P. aeruginosa* or from genus *Escherichia* preferably *E. coli.*

[0141] In another preferred embodiment of the medical use of a compound of formula (II) as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, the infection is caused by a fungus. In a more preferred embodiment, the fungus is selected from genus *Candida, Aspergillus, Saccharomyces* or *Scedosporium.* In an even more preferably embodiment, the fungus from genus *Candida* is *C. albicans, C. glabrata, C. tropicalis, C. lusitaniae, C. guilliermondi* or *C. parapsilopsis,* the fungus from genus *Aspergillus* is *A. fumigatus, A. flavus* , *A. niger* or *A. terreus* and the fungus from genus *Scedosporium* is *S. prolificans.*

[0142] In another preferred embodiment, the fungus is selected from genus *Candida, Aspergillus* or *Saccharomyces.*

[0143] In another preferred embodiment, the fungus from genus *Candida* is *C. albicans, C. parapsilopsis, C. tropicalis, C. lusitaniae, C. guilliermondi,* the fungus from genus *Aspergillus* is *A. fumigatus, A. flavus, A. niger* or *A. terreus* and/or the fungus from *Saccharomyces* is *S. cerevisiae.*

[0144] In another preferred embodiment of the medical use of a compound of the invention as defined above, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof, the infection is caused by a virus.

[0145] The term "virus", refers to a small infectious agent that replicates only inside the living cells of other organism.

[0146] In some embodiments, and without limitation, the virus is selected from the group consisting of adenovirus, coxsackievirus, Epstein-Bar, Hepatitis A, B or C, herpes simplex type 1, herpes simplex type 2, cytomegalovirus, herpesvirus type 8, HIV, Influenza, Measles, mumps, human papillomavirus, parainfluenza, poliovirus, rabies, respiratory syncytial, rubella, varicella-zoster. In a preferred embodiment the virus is selected from HIV, herpes simplex I, herpes simplex II, Suid herpesvirus 1 or Equine herpesvirus 1.

[0147] In a more preferred embodiment, the virus is HIV.

[0148] The present invention covers any combination of compounds and diseases.

[0149] For use in the prevention and/or treatment according to the invention, the compound of the invention or a pharmaceutically acceptable salt, solvate or isomer thereof or the pharmaceutical composition of the invention is present in an effective amount.

[0150] The term "effective" amount or a "therapeutically effective amount" of a drug or pharmacologically active agent is meant a nontoxic but sufficient amount of the drug or agent to provide the desired effect. In the combination therapy of the present invention, an "effective amount" of one component of the combination is the amount of that compound that is effective to provide the desired effect when used in combination with the other components of the combination.

[0151] Even though individual needs vary, determination of optimal ranges for effective amounts of the agent of the invention belongs to the common experience of those experts in the art. In general, the dosage needed to provide an effective amount of such compound, which can be adjusted by one expert in the art will vary depending on age, health,

fitness, sex, diet, weight, frequency of treatment and the nature and extent of impairment or illness, medical condition of the patient, route of administration, pharmacological considerations such as activity, efficacy, pharmacokinetic and toxicology profile of the particular compound used, if using a system drug delivery, and if the compound is administered as part of a combination of drugs.

[0152] The effective quantity of the compound of the invention can vary within a wide range and, in general, will vary depending on the particular circumstances of application, duration of the exposure and other considerations. In a particular embodiment, the dose ranges between 0.05 mg/kg and 50 mg/kg, more preferably between 1 mg/kg and 20 mg/kg.

[0153] In a preferred embodiment the effective amount is between about between about 0.005 % and about 0.04% weight, between about 0.0075 % weight and about 0.0375 % weight, between about 0.001 % weight and about 0.035 % weight, between about 0.00125 % weight and about 0.0325 % weight, between about 0.0015 % weight and about 0.0325 % weight, between about 0.00175 % weight and about 0.03 % weight, and more preferably between about 0.0018 % weight and about 0.032 % weight. In a particular embodiment, the effective amount is between about 0.005% and about 0.02% weight, preferably between about 0.005% weight and about 0.015% weight, more preferably between about 0.005% weight and about 0.01% weight. In some embodiments the effective amount is about 0.001 % weight, about 0.002 % weight, about 0.003 % weight or about 0.004 % weight. The percentages (% w/w) are expressed as weight of the compound of the invention or a pharmaceutically acceptable salt, solvate or isomer thereof by the total weight of the composition comprising the compound or by weight of the foodstuff, foodstuff package, medical device or surface.

[0154] In another embodiment the effective amount is expressed in μg/mL or μg/g (μg of the compound of the invention or a pharmaceutically acceptable salt, solvate or isomer thereof by mL or g of the composition comprising the compound), therefore effective amount is about 75 and about 375 μg/mL (or μg/g), between about 100 and about 350 μg/mL (or μg/g), between about 125 and about 325 μg/mL (or μg/g), between about 150 and about 325 μg/mL (or μg/g), between about 175 and about 300 μg/mL (or μg/g), and more preferably between about 180 and about 320 μg/mL (or μg/g). In a particular embodiment, the effective amount is between about 50 and about 200 μg/mL (or μg/g), preferably between 50 and about 150 μg/mL (or μg/g), more preferably between about 50 and about 100 μg/mL (or μg/g). In some embodiments the effective amount is about 100 μg/mL (or μg/g), about 200 μg/mL (or μg/g), about 300 μg/mL (or μg/g) or about 400 μg/mL (or μg/g).

[0155] When the compound of the invention or a salt, solvate or isomer thereof as defined herein is present on a surface, it is preferably in an effective amount of between about 1 and about 200 $\mu g/cm^2$, preferably between about 1 and about 100 $\mu g/cm^2$, preferably between about 1 and about 50 $\mu g/cm^2$, more preferably between about 5 and about 300 $\mu g/cm^2$.

[0156] The invention will be described by way of the following examples which are to be considered as merely illustrative and not limitative of the scope of the invention.

Materials and methods

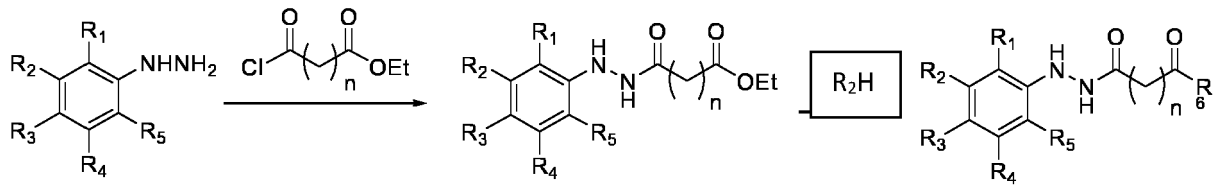
Synthesis process of some compounds belonging to the invention

Step 1

[0157] The various phenylhydrazines (2.5 mmol, 2 eq) and ethyl chlorooxoacetate or malonate (1.25 mmol, 1 eq) were dissolved in CH_2Cl_2. The reaction mixture was stirred at 0°C for 10-15 min. The reaction was extracted with HCl (10%). The combined organic phase was dried over $MgSO_4$ and concentrated. After removal of the solvent, a solid 7 (a- ...) (depending on the phenylhydrazine derivative) was obtained.

Step 2

[0158] Compound **7** (1 eq) and R_2H (1 eq) were dissolved in MeOH. The reaction mixture was stirred at room temperature for 12h. A precipate of **8** was filtered off and washed with cold methanol.



6 **7** **8**

Bacterial strains and inoculum preparation

[0159] Bacterial strains, from clinical origin, were supplied by the National Center for Microbiology, Institute of Health Carlos III (Majadahonda, Madrid). They are detailed in Table I.

Table I. Characteristics of strains.

Specie	Strain	Isolation year	IMP	CTX	A/C	LIN	AMK	SxT	CIP	ERI	PEN	VAN	RIF	TET	CLI	MER	CEF	TOB	GEN
N. cyriacigeorgica	30	2005	S	S	R	S	S	S	R	R									
N. cyriacigeorgica	199	2005	R	R	R	S	R	S	R	R									
N. carnea	769	2009	S	S	S	S	S	R	S	R									
N. carnea	40	2011	R	S	S	S	R	R	S	R									
T. pulmonis	1991	2009	S	S	S	S	S	S	S	S									
T. pulmonis	40	2015	S	R	R	R	R	R	R	R									
M. chelonae	870	2011	R			R		R	R	R	R								
M. abscessus	690	2012	R			S		S	R	S	R								
M. fortuitum	1080	2011	R			R		S	S	R	R								
B. cereus	25	2014								R	S	S	S	R	R				
B. cereus	182	2013								R	S	S	S	S	R				
A. baumannii	300	2001	R				R		R							R	R	S	
A. baumannii	1301	2009	S				S		S							S	R	s	
S. aureus	282	2005					S		R	R		S		S	R				R
S. aureus	890	2010					S		S	R		S		R	R				R
S. epidermidis	982	2006					S		R	R		S		S	R				R
S. epidermidis	188	2009					S		S	S		S		S	S				S
E. faecium	209	2015		R			R				R	S							S
E. faecium	26	2012		R			S				R	I							S
E. faecalis	1052	2008		R			S				R	S							S
E. faecalis	52	2006		R			S				R	S							S
P. aeruginosa	96	2014		S			S		R							S	R	s	
P. aeruginosa	115	2013		S			S		S							R	R	s	
E. coli	29	2012	S	S	S		S			S	R								S

(continued)

Specie	Strain	Isolation year	IMP	CTX	A/C	LIN	AMK	SxT	CIP	ERI	PEN	VAN	RIF	TET	CLI	MER	CEF	TOB	GEN
E. coli	305	2008	S	R	R		S			S	R								S

[0160] IMP=Imipenem; CTX=Cefotaxime; A/C=Amoxicillin/Clavulanate; Lin=Linezolid; AMK=Amikacin; SxT=Cotrimoxazole; CIP=Ciprofloxacin; ERI=Erythromycin; PEN=Penicillin; VAN=Vancomycin; RIF=Rifampicin; TET=Tetracycline; CLI=Clindamycin; MER=Meropenem; CEF=Ceftriazone; TOB=Tobramycin; GEN=Gentamicin; R= resistant, S=susceptibility

Antibacterial susceptibility test

[0161] Bacterial cells suspension in sterile saline was prepared from a culture of 24-72 h, depending on bacterial species, in Mueller-Hinton Agar with 5% sheep blood. Each suspension was adjusted to a fixed size inoculum of 1-5 x 10^8 CFU/ml with a spectrophotometer (Ferraro, MJ National Committee for Clinical Laboratory Standards. 2000).

[0162] Kirby-Bauer disk diffusion susceptibility test protocol was utilized to determine the sensitivity or resistance of pathogenic bacteria against the compounds and others antibiotics. The absence of growth around the disks is an indirect measure of the ability of this compound to inhibit an organism (Kirby, W.. et al., Antibiotics Annu. 1956-1957:892). After 18 to 72 hours of incubation at 37°C, with or without CO_2, under aerobic or anaerobic conditions, depending on the bacterial species, halo of growth inhibition were obtained and evaluated.

Antibiotic activity

[0163] Interpretation of susceptibility and resistance was based on the presence or absence of a zone of inhibition surrounding the disk. Kirby-Bauer disk diffusion susceptibility test is a common method which uses antibiotic-impregnated wafers to test whether bacteria are affected by antibiotics. The size of the zone of inhibition depends on how effective the antibiotic is at stopping the growth of the bacterium. A stronger antibiotic will create a larger zone, because a lower concentration of the antibiotic is enough to stop growth.

[0164] The results of antibiotic activity obtained with the Kirby-Bauer antibiotic test show the great potential of compounds, not only as molecules with specific activity against specific bacteria but also as possible structures for the development of broad spectrum antibiotics. The activity results are shown in Tables II- VIII and Figure 1 (it has to be noted that MSG196 does not form part of the invention).

[0165] All compounds were tested at 300 μg/disc.

Table II. MSG-116

	Activity detected (mm) 300 ng/disc
Species	**MSG-196**
N. cyriacigeorgica	34
N. cornea	30
T. pulmonis	22
S. pneumoniae	20
S. pyogenes	20
K. pneumoniae	13
C. difficile	18

Table III. MSG-210

	Activity detected (mm) 300 μg/disc
Species	**MSG-210**
N. cyriacigeorgica	15
N. cornea	11
T. pulmonis	20
A. baumannii	18

Table IV. MSG-218

	Activity detected (mm)
Species	**MSG-218**
T. pulmonis	33
A. baumannii	15

Table V. MSG-214

	Activity detected (mm) 300 μg/disc
Species	**MSG-214**
N. cyriacigeorgica	25
N. cornea	14
T. pulmonis	30
S. pneumoniae	11
A. baumannii	12

Table VI. MSG-216

	Activity detected (mm) 300 μg/disc
Species	**MSG-216**
N. cyriacigeorgica	17
N. cornea	14
T. pulmonis	25
K. pneumoniae	11
A. baumannii	12

Table VII. MSG-119

	Activity detected (mm), 300 μg/disc
Species	**MSG-119**
A. baumannii	20
P. aeruginosa	15

Table VIII. MSG-213 and MSG-235

	300 μg	
Species	**MSG-231**	**MSG-235**
N. cyriacigeorgica	33	29
N. cornea	38	34
T. pulmonis	27	24
M. abscessus	27	23
C. difficile	24	20

(continued)

	300 μg	
Species	**MSG-231**	**MSG-235**
E. faecium	27	22
E. faecalis	29	25
S. pneumoniae	24	21
S. epidermidis	33	27
K. pneumoniae	10	12
E. cloacae	10	11
A. baumannii	20	15
P. aeruginosa	11	11
E. coli	17	14

Example 2-ANTIFUNGAL ACTIVITY

Filamentous fungi and yeasts strains and inoculum preparation

[0166] Filamentous fungi and yeasts strains, from clinical origin, were supplied by Microbiology Service from The Princess Hospital, Madrid. They are detailed in Table IX.

Table IX. Characteristics of the strains.

yeast / fungus	**Amphotericin B**	**Ketoconazole**	**Itraconazole**	**Clotrimazole**	**Fluconazole**
C.albicans	**I**	5	**R**	5	S
C. glabrata	5	5	I	5	S
C. tropicalis	5	5	I	5	S
C. parapsilosis	5	5	**S**	5	S
C. lusitaniae	**I**	5	5	5	S
C. Krusei	**I**	5	**R**	5	S
C. guillermondii	**R**	**R**	**R**	**R**	**R**
A. fumigatus	5	5	I	5	**R**
A. niger	5	5	I	5	**R**
A. terreus	I	5	I	**S**	**R**
A. flavus	I	5	I	**S**	**R**
S. cerevisiae	I	5	5	**R**	5
I=intermediate activity; S=susceptibility; R=Resistance					

[0167] Filamentous fungi and yeast cells suspensions in distilled water was prepared from a culture of 24-48 h, depending on species, in Sabouraud agar. Each suspension was adjusted to a fixed size inoculum of 1-5 x 10^8 CFU/ml with a spectrophotometer (Ferraro, MJ National Committee for Clinical Laboratory Standards. 2000).

Antifungal susceptibility test

[0168] Antifungal susceptibility tests were developed following the standardized methodology detailed in document CLSI: M44-4: Method for Antifungal Disk diffusion susceptibility testing of yeasts consisting of disk diffusion on agar Muller-Hinton (supplemented with 2 % glucose).

Antifungal activity:

[0169] The activity results are shown in Table X. The compound was tested at 150 and 500 μg/disc. A great activity was exhibited in fungi strains and in *Candida* spp. (Table X and Figures 2 to Figure 8).

Table X. Antifungal activities detected with the compounds.

	Activity (mm)																	
Species	**MSG-187**		**MSG-193**		**MSG-119**		**Ket *50 μg***	**MSG-210**		**MSG-214**		**MSG-216**		**MSG-218**		**MSG-227**		**Clo 10 μg**
μg/disc	**150**	**500**	**150**	**500**	**150**	**500**		**150**	**500**	**150**	**500**	**150**	**500**	**150**	**500**	**150**	**500**	
C. albicans	min	22	20	>40	21	24	22	32	>40	40	>40	24	>40	24	>40	26	>40	15
C. parapsilosis	min	17	18	>40	15	>40	42	28	32	15	>40	11	>40	25	36	31	>40	42
C. lusitaniae	min	20	15	>40	min	20	41	39	>40	42	>40	36	>40	22	46	>40	>40	41
C. guillermondii	min	22	20	40	12	>40	44	32	35	15	>40	13	>40	22	40	>40	>40	44
C. tropicalis	min	18	30	>40	20	>40	25	34	36	34	>40	26	>40	10	40	26	>40	25
S. cerevisiae	min	min	22	40	26	35	30	28	30	15	32	19	35	24	34	20	25	30
A. niger	min	40	15	>40	24	>40	25	27	40	10	>40	10	36	22	30	32	>40	25
A. flavus	min	36	15	>40	18	>40	32	10	9	min	min	min	min	min	min	25	>40	32
A. fumigatus	min	32	20	>40	22	>40	22	10	16	min	16	min	10	min	10	11	>40	22
A. terreus	min	min	12	32	20	>40	26	19	22	min	17	min	10	min	10	>40	>40	26
Min: minimum detected activity (halo diameter <10 mm); ket: ketoconazole; Clo: clotrimazol																		

Example 3-Anti-HIV activity

Antiviral susceptibility test

[0170] Assessment of *in vitro* antiviral activity is usually performed to estimate parameters of antiviral potency and efficacy represented by the percentage of inhibition of HIV activity or IC50. The assay utilized is based on the use of recombinant viruses in which the nef gene, essential for *in vitro* HIV replication, has been replaced by a Renilla reporter gene so that viral replication can be quantified directly (Garcia-Perez J et al, J Med Virol. 2007 Feb;79(2):127-37). The assay was performed infecting MT-2 cells or PHA-activated PBMCs / IL-2 with viral supernatants obtained previously. The study was development in AIDS Immunopathology Unit, Nacional Center of Microbiology, Institute of Health Carlos III, Majadahonda, Madrid, Spain.

Viability

[0171] All assays for assessing anti-HIV activity were taken in parallel to determine cellular viability of the culture in the presence or absence of different concentrations of the isolated molecule. It was followed exactly the same methodology as in the anti-HIV assay except with the addition of complete DMEM medium instead of supernatant viral, in the same proportion, and the detection of the viability was performed with the viability detection kit CellTiter Glo (Promega), following manufacturer instructions. Viability is directly proportional to the luciferase activity obtained.

[0172] All data are expressed as percentage relative to a control with DMSO at the same concentration. Antiviral activity and toxicity curves were performed to the compound at different concentrations.

Results

[0173] The profile of activity/toxicity of the compounds was good with an intrinsic activity in the micromolar range medium (Figure 9). The safety index value is more than 100 for all of them. As an example, IC50 value of MSG-119 is in the micromolar range (IC50 of 7, 11 μM) (Table XI).

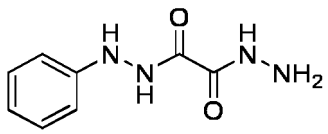
Table XI. IC50 (half maximal inhibitory concentration) of the compound. 95% confidence interval (CI95%). CC50 means concentration of drug required to kill 50% of cells. The value R2 is a measure of goodness-of-fit of linear regression (using graphPad prism).

	IC_{50} VIH MT-2 μM	**CI95%**	**R^2**	**CC_{50} VIH MT-2 μM**	**CI95%**	**R^2**
MSG-119	**7,11**	2,50 to 20,22	0,8604	**>10**	-	-

Characterization of the compounds

MSG119

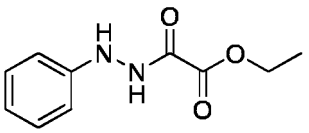
[0174]



[0175] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.53 (d, *J* = 1.6 Hz, 1H), 10.09 (s, 1H), 7.81 (d, *J* = 1.6 Hz, 1H), 7.16-7.11 (m, 2H), 6.74-6.67 (m, 3H), 4.56 (bs, 2H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 159.7, 157.8, 148.5, 128.6, 118.7, 112.3.

MSG156 (Reference Example)

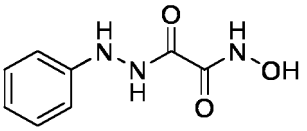
[0176]



[0177] ^{1}H NMR ($CDCl_3$, 300 MHz, ppm): δ 8.73 (s, 1H), 7.19-7.16 (m, 2H), 6.89-6.84 (m, 1H), 6.78-6.76 (m, 2H), 6.15 (bs, 1H), 4.32 (q, 2H), 1.33 (t, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ 159.7, 156.2, 146.5, 129.3, 121.9, 114.0, 63.5, 14.0.

MSG158

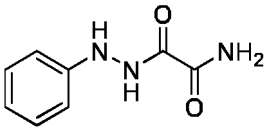
[0178]



[0179] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 11.56 (s, 1H), 10.55 (s, 1H), 9.25 (bs, 1H), 7.79 (bs, 1H), 7.16-7.12 (m, 2H), 6.74-6.68 (m, 3H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 159.7, 157.8, 148.5, 128.6, 118.7, 112.3.

MSG159 (Reference Example)

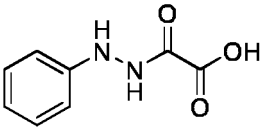
[0180]



[0181] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.50 (s, 1H), 8.10 (s, 1H), 7.83 (s, 1H), 7.78 (s, 1H), 7.17-7.12 (m, 2H), 6.74-6.69 (m, 3H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 161.9, 160.2, 148.5, 128.6, 118.8, 112.3.

MSG160 (Reference Example)

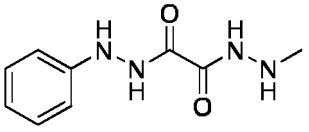
[0182]



[0183] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.60 (s, 1H), 7.18-7.13 (m, 2H), 6.75-6.71 (m, 3H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 161.9, 158.6, 148.4, 128.7, 118.9, 112.4

MSG.161

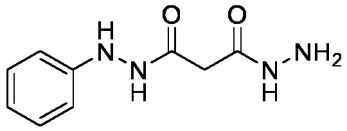
[0184]



[0185] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.33 (s, 1H), 7.82 (s, 1H), 7.18-7.12 (m, 2H), 6.75-6.68 (m, 3H), 2.51 (s, 3H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 159.9, 157.4, 148.4, 128.8, 118.9, 112.4, 38.0.

MSG187

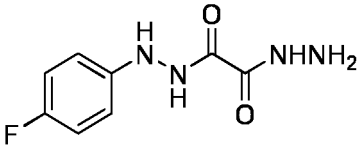
[0186]



[0187] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 9.67 (s, 1H), 9.13 (s, 1H), 7.72 (s, 1H), 7.14-7.09 (m, 2H), 6.76-6.68 (m, 3H), 4.26 (s, 1H), 3.04 (s, 2H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 166.4, 165.8.4, 149.0, 128.5, 118.4, 112.1, 40.2

MSG193

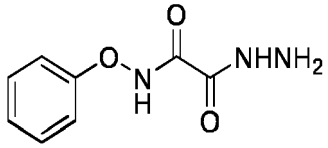
[0188]



[0189] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.56 (bs, 1H), 10.08 (bs, 1H), 7.78 (s, 1H), 6.98 (d, *J* = 7.0 Hz, 2H), 6.70 (d, *J* = 7.0 Hz, 2H), 4.56 (s, 2H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 160.2, 158.2, 156.4 (d, *J* = 234 Hz), 145.5, 115.5 (d, *J* = 22 Hz), 114.1 (d, *J* = 7.5 Hz)

MSG.196 (Reference Example)

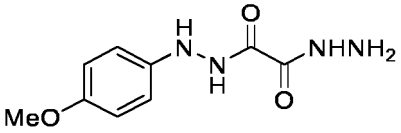
[0190]



[0191] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): 7.19 (t, J=7.8 , 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 7.2 Hz, 2H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 159.9, 157.4, 148.4, 128.8, 118.9, 112.4

MSG210

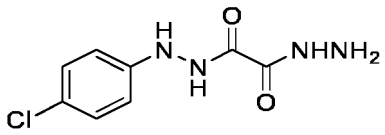
[0192]



[0193] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.48 (s, 1H), 10.05 (s, 1H), 7.48 (s, 1H), 6.75-6.69 (m, 4H), 4.54 (s, 2H), 3.66 (s, 3H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 166.4, 165.8, 149.0, 128.5, 118.4, 112.1, 40.2

MSG214

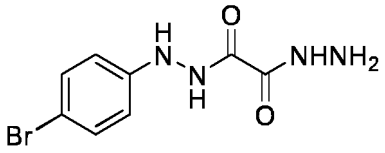
[0194]



[0195] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.60 (s, 1H), 10.10 (s, 1H), 8.00 (s, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.69 (d, J= 8.7 Hz, 2H), 4.55 (s, 2H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 159.7, 157.6, 147.5, 128.4, 122.0, 113.8.

MSG216

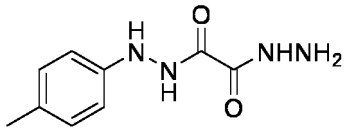
[0196]



[0197] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.60 (s, 1H), 10.11 (s, 1H), 8.02 (s, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.64 (d, *J* = 8.5 Hz, 2H), 4.55 (s, 2H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 159.7, 157.6, 147.9, 131.3, 114.2, 109.5.

MSG218

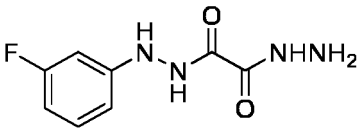
[0198]



[0199] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.45 (bs, 1H), 10.06 (bs, 1H), 7.62 (s, 1H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.61 (d, *J* = 7.8 Hz, 2H), 4.55 (s, 2H), 2.17 (s, 3H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 159.6, 157.8, 146.2, 129.0, 127.4, 112.6, 20.1.

MSG227

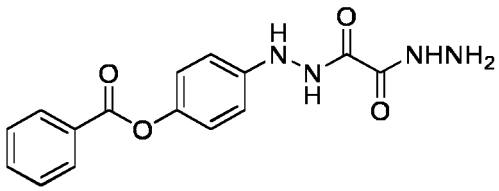
[0200]



[0201] ^{1}H NMR (DMSO-d^{6}, 300 MHz, ppm): δ 10.60 (bs, 1H), 10.12 (bs, 1H), 8.13 (s, 1H), 7.19-7.11 (m, 1H), 6.53-6.39 (m, 3H), 4.55 (s, 2H). ^{13}C NMR (DMSO-d^{6}, 75 MHz, ppm): δ 163.0 (d, *J* = 242Hz), 159.7, 157.6, 130.3 (d, *J* = 10.2 Hz), 108.2, 104.7 (d, *J* = 22Hz), 98.7 (d, *J* = 26.8 Hz).

MSG231

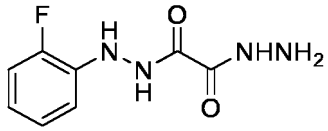
[0202]



^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.61 (bs, 1H), 10.11 (bs, 1H), 8.12-8.09 (m, 2H), 7.93 (s, 1H), 7.76-7.71 (m, 1H), 7.62-7.57 (m, 2H), 7.05 (d, J=8.1 Hz, 2H), 6.75 (d, *J* = 8.1 Hz, 2H), 4.56 (s, 2H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 165.0, 159.8, 157.8, 146.5, 143.0, 133.8, 129.6, 128.9, 121.9, 112.8.

MSG235

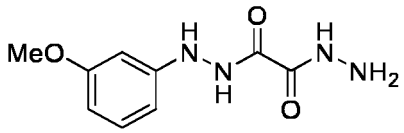
[0203]



[0204] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.6 (bs, 1H), 10.11 (bs, 1H), 7.75 (s, 1H), 7.11-6.96 (m, 2H), 6.73-6.67 (m, 2H), 4.56 (s, 2H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 159.8, 157.6, 150.2 (d, *J* = 239.5 Hz), 136.1 (d, *J* = 9.8 Hz), 124.5 (d, *J*= 3 Hz), 118.9 (d, *J* = 7 Hz), 114.8 (d, *J* = 18 Hz), 113.6 (d, *J* = 3 Hz).

MSG.237

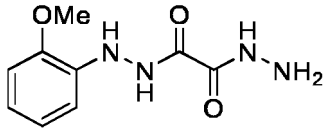
[0205]



[0206] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.5 (bs, 1H), 10.08 (bs, 1H), 7.81 (s, 1H), 7.06-7.01 (m, 1H), 6.31-6.24 (m, 3H), 4.57 (s, 2H), 3.67 (s, 3H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 160.5, 160.2, 158.2, 150.4, 130.0, 105.6, 104.6, 98.7, 55.2

MSG.239

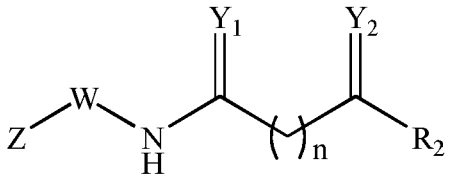
[0207]



[0208] ^{1}H NMR (DMSO-d^6, 300 MHz, ppm): δ 10.6 (bs, 1H), 10.08 (bs, 1H), 7.03 (s, 1H), 6.88-6.61 (m, 4H), 4.56 (s, 2H), 3.81 (s, 3H). ^{13}C NMR (DMSO-d^6, 75 MHz, ppm): δ 159.4, 157.6, 146.5, 137.3, 120.6, 119.3, 111.6, 110.5, 55.5

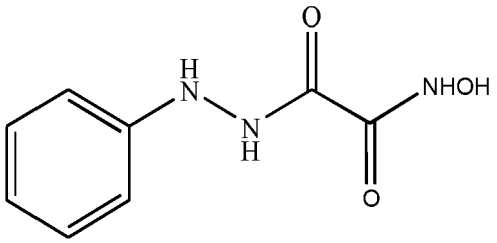
Claims

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof,
wherein
Y_1= O;
Y_2= O;
W= NH;
n= 0, 1;
R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups; Z= 1-pyridine, 2-pyridine, 3-pyridine or phenyl, wherein the phenyl is optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl, aryl, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$, wherein the term "alkyl" includes cyclic groups, with the proviso that when Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ and W is NH then Z is not a group selected from the group consisting of a pyridine group, and a phenyl group wherein the phenyl group is optionally substituted with methyl, halogen, NO_2 or OCH_3 group and with the proviso that the compound is not



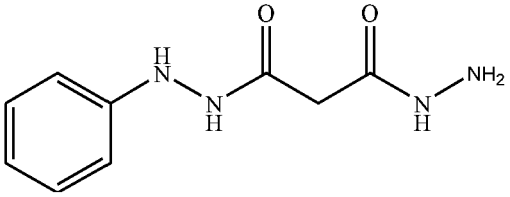
.

2. The compound as defined in claim 1, wherein R_2 is $NH-NH_2$ and/or wherein n is 1 and Y_1=Y_2= O.

3. The compound as defined in claim 1 or 2 , wherein Z is a phenyl group optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NHNH_2$, $-NH-CH_3$ and $-NR_6R_7$, , wherein R_5 is C_{1-6} alkyl, aryl or hydrogen wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, $-OC(O)R_5$, or $-C(O)OR_5$.

4. The compound as defined in claim 1 wherein R_4 is selected from the group consisting of $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups.

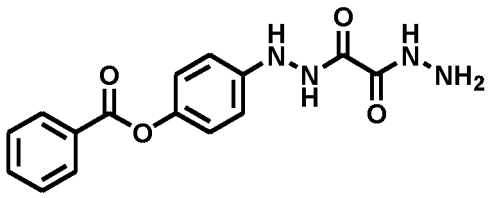
5. The compound as defined in claim 1, having the following formula:



,

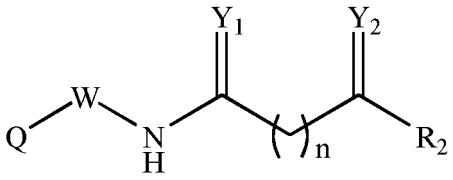
(Ia) MSG187

or



(Ig) MSG231

6. A compound of formula (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof,
wherein
Y_1= O;
Y_2= O;
W= NH;
n = 0, 1;
R_2= NHR_4, wherein R_4 is selected from the group consisting of OH, $-NH_2$, $-NH-CH_3$ and $-NR_aR_b$, wherein R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups;
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, -NHOH, $-NH-NH_2$, $-NH-CH_3$ and $-NR_6R_7$, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs-, $-OC(O)R_5$, or $-C(O)OR_5$,
c) 5-6 membered aromatic ring having one or more heteroatoms selected from the group consisting of N, S, and O and being optionally substituted with one or more groups independently selected from the group consisting of:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- (C_{1-6}alkyl)OCHz-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$, and $-C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,

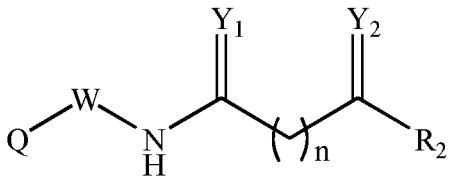
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,
- (C_{1-6}alkyl)OCH_2-,

- C_{1-6} alkoxy,

- OH, -SH or -SR_5 wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- -NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, -C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, and
- $NHC(O)R_5$-, -C(O)NH-R_5, -$OC(O)R_5$, and -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,

wherein the term "alkyl" includes cyclic groups and with the proviso that when Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ and W is NH then Q is not a phenyl group, or a pharmaceutical composition comprising said compound and a pharmaceutically acceptable excipient for use in medicine.

7. A pharmaceutical composition comprising a compound of formula (II)



(II)

or a pharmaceutically acceptable salt, stereoisomer or solvate thereof,
wherein
Y_1= O;
Y_2= O;
W= NH
n= 0, 1;
R_2= NHR_4, and wherein R_4 is selected from OH, -NH_2, -NH-CH_3 and -NR_aR_b, wherein
R_a and R_b are independently selected C_{1-6} alkyl groups or aryl groups,
Q is selected from a group consisting of:

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) phenyl optionally substituted with one or more groups independently selected from C_{1-8} alkyl, C_{2-8} alkenyl, halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -$C(O)OR_5$, - $OC(O)R_5$, CF_3, CN, NH_2, -NHOH, -NH-NH_2, -NH-CH_3 and -NR_6R_7, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen, wherein R_6 and R_7 are independently selected C_{1-6} alkyl groups, aryl groups, -C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$-,.
c) 5-6 membered aromatic ring having one or more heteroatoms selected from N, S, and O and being optionally substituted with one or more groups independently selected from:

- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group having one or more heteroatoms selected from N, S, and O,
- halogen,
- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- NR_aR_b, wherein R_a and R_b are independently selected from C_{1-6} alkyl groups or aryl groups, and
- $NHC(O)R_5$-, -C(O)NH-R_5, -$OC(O)R_5$, and -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and

d) a fused bicyclic ring containing at least one phenyl group and a C_{5-6} aromatic heterocyclic group having one or more heteroatoms selected from N, S, and O, wherein the phenyl group of said fused bicyclic ring is optionally substituted with one or more groups independently selected from

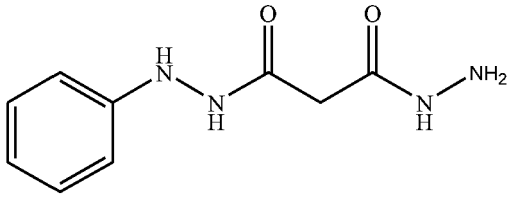
- C_{1-8} alkyl, linear or branched C_{1-8} alkenyl, C_{5-6} cycloalkyl,
- phenyl as defined in b),
- 5-6 membered aromatic ring group as defined in c),
- halogen,

- (C_{1-6}alkyl)OCH_2-,
- C_{1-6} alkoxy,
- OH, -SH or -SR_5 wherein R_5 is C_{1-6} alkyl, aryl or hydrogen,
- NR_6R_7, wherein R_6 and R_7 are independently selected from C_{1-6} alkyl groups, aryl groups, C(O)Rs, -$OC(O)R_5$, or -$C(O)OR_5$, wherein R_5 is C_{1-6} alkyl, aryl or hydrogen, and
- $NHC(O)R_5$-, -$C(O)NH$-R_5, -$OC(O)R_5$, or -$C(O)OR_5$-, wherein R_5 is C_{1-6} alkyl, aryl, or hydrogen,

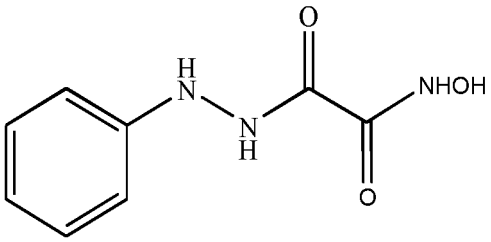
wherein the term "alkyl" includes cyclic groups, and a pharmaceutically acceptable excipient for use in the prevention and/or treatment of an infection caused by a fungus.

8. A pharmaceutical composition for use according to any of claims 6 or 7 wherein Y_1=Y_2=O\, n= 0, and Q is a phenyl group optionally substituted in para position with a group selected from the group consisting of H, halogen, CH_3 and OCH_3.

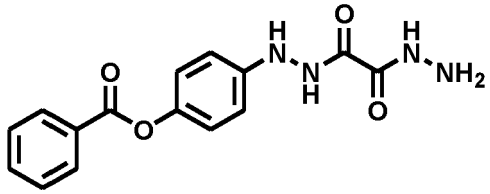
9. A pharmaceutical composition for use according to claim 7 wherein the compound is selected from the group consisting of



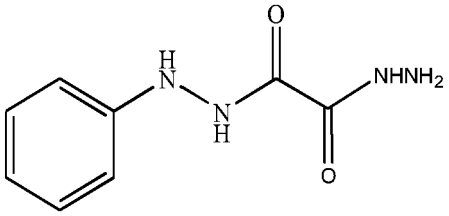
(Ia) MSG187



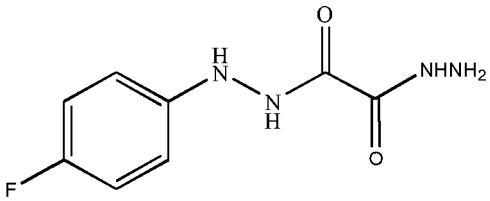
(Ib) MSG158



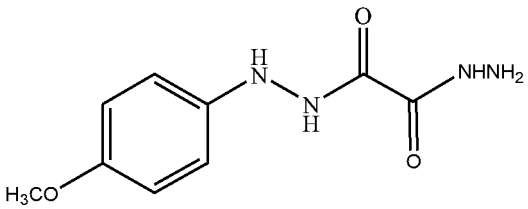
(Ig) MSG231



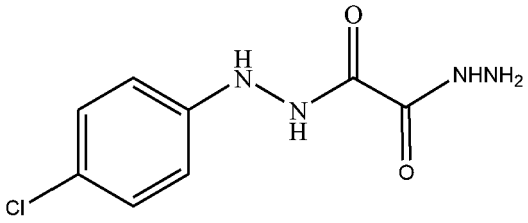
(IIa)MSG119



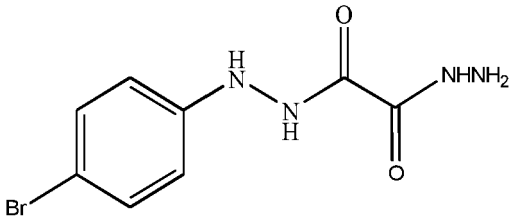
(IIb) MSG193



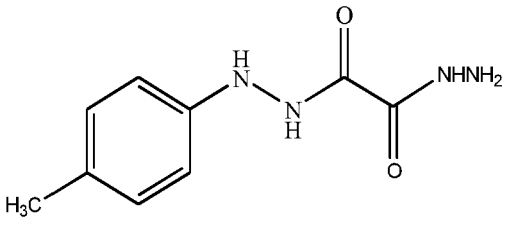
(IIc) MSG210



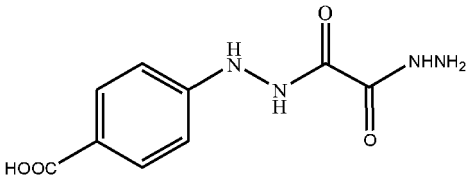
(IId) MSG214



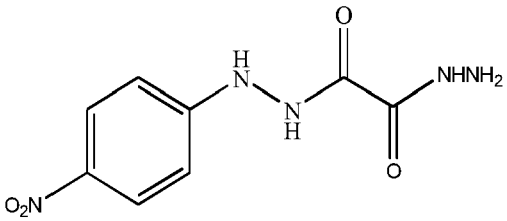
(IIe) MSG216



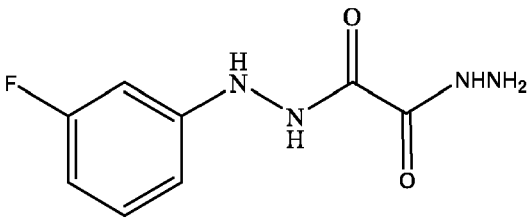
(IIf) MSG218



(IIg) MSG223

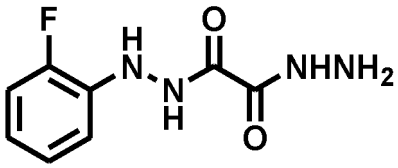


(IIh) MSG198



(IIi) MSG 227

and



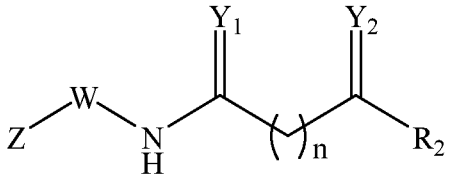
(IIj) MSG235

10. The pharmaceutical composition for use according to any of claims 7 to 9 wherein the fungus is selected from genus *Candida, Aspergillus* or *Saccharomyces.*

11. The pharmaceutical composition for use according to claim 10 wherein the fungus from genus *Candida* is *C. albicans, C. parapsilopsis, C. tropicalis, C. lusitaniae, C. guilliermondi,* the fungus from genus *Aspergillus* is *A. fumigatus, A. flavus, A. niger* or *A. terreus* and/or the fungus from *Saccharomyces* is *S. cerevisiae.*

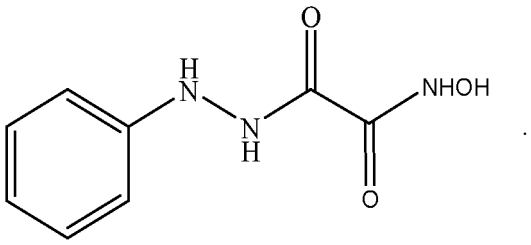
Patentansprüche

1. Verbindung der Formel (I):



(I)

oder ein pharmazeutisch verträgliches Salz, Stereoisomer oder Solvat davon, wobei
Y_1= O;
Y_2= O;
W= NH;
n= 0, 1;
R_2= NHR_4, wobei R_4 ausgewählt ist aus der Gruppe bestehend aus OH, $-NH_2$, $-NH-CH_3$ und $-NR_aR_b$, wobei R_a und R_b unabhängig voneinander ausgewählte C_{1-6}-Alkylgruppen oder Arylgruppen sind;
Z= 1-Pyridin, 2-Pyridin, 3-Pyridin oder Phenyl, wobei das Phenyl gegebenenfalls mit einer oder mehreren Gruppen substituiert ist, die unabhängig voneinander aus der Gruppe ausgewählt sind, die aus C_{1-8}-Alkyl, C_{2-8}-Alkenyl, Halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ und $-NR_6R_7$, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, wobei R_6 und R_7 unabhängig voneinander ausgewählt sind aus C_{1-6}-Alkyl, Aryl, -C(O)Rs, -OC(O)Rs oder $-C(O)OR_5$, wobei der Begriff "Alkyl" zyklische Gruppen einschließt, mit der Maßgabe, dass wenn Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ und W NH ist, dann ist Z nicht eine Gruppe, ausgewählt aus der Gruppe, bestehend aus einer Pyridingruppe und einer Phenylgruppe, wobei die Phenylgruppe gegebenenfalls mit einer Methyl-, Halogen-, NO_2- oder OCH_3-Gruppe substituiert ist, und mit der Maßgabe, dass die Verbindung nicht



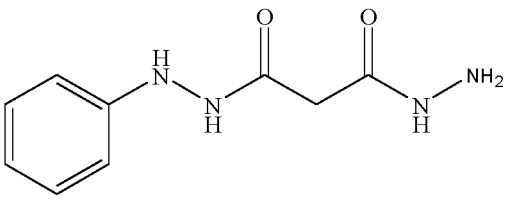
ist.

2. Verbindung nach Anspruch 1, worin R_2 $NH-NH_2$ ist und/oder wobei n 1 ist und Y_1=Y_2= O.

3. Verbindung nach Anspruch 1 oder 2, wobei Z eine Phenylgruppe ist, die gegebenenfalls mit einer oder mehreren Gruppen substituiert ist, die unabhängig voneinander aus der Gruppe ausgewählt sind, die aus C_{1-8}-Alkyl, C_{2-8}-Alkenyl, Halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, -C(O)ORs, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NHNH_2$, $-NH-CH_3$ und $-NR_6R_7$, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, wobei R_6 und R_7 unabhängig voneinander aus C_{1-6}-Alkylgruppen, Arylgruppen, -C(O)Rs, -OC(O)Rs oder -C(O)ORs ausgewählt sind.

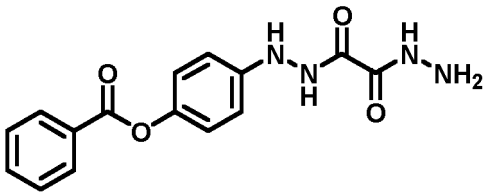
4. Verbindung nach Anspruch 1, wobei R_4 ausgewählt ist aus der Gruppe bestehend aus $-NH_2$, $-NH-CH_3$ und $-NR_aR_b$, wobei R_a und R_b unabhängig voneinander aus C_{1-6}-Alkylgruppen oder Arylgruppen ausgewählt sind.

5. Verbindung, wie in Anspruch 1 definiert, mit der folgenden Formel:



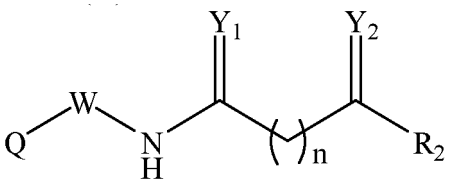
(Ia) MSG187

oder



(Ig) MSG231

6. Verbindung der Formel (II):



(II)

oder ein pharmazeutisch verträgliches Salz, Stereoisomer oder Solvat davon, wobei
Y_1= O;
Y_2= O;
W= NH;
n = 0, 1;
R_2= NHR_4, wobei R_4 ausgewählt ist aus der Gruppe bestehend aus OH, $-NH_2$, $-NH-CH_3$ und $-NR_aR_b$, wobei R_a und R_b unabhängig voneinander ausgewählte C_{1-6}-Alkylgruppen oder Arylgruppen sind;
Q ausgewählt ist aus einer Gruppe, bestehend aus:

a) 1-Pyridin, 2-Pyridin, 3-Pyridin,
b) Phenyl, gegebenenfalls substituiert mit einer oder mehreren Gruppen, unabhängig ausgewählt aus der Gruppe, bestehend aus C_{1-8}-Alkyl, C_{2-8}-Alkenyl, Halogen, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, -NHOH, $-NH-NH_2$, $-NH-CH_3$ und $-NR_6R_7$, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, wobei R_6 und R_7 unabhängig voneinander aus C_{1-6}-Alkylgruppen, Arylgruppen, -C(O)Rs-, -OC(O)Rs oder -C(O)ORs ausgewählt sind,
c) 5-6-gliedriger aromatischer Ring mit einem oder mehreren Heteroatomen, ausgewählt aus der Gruppe, bestehend aus N, S und O, und gegebenenfalls substituiert mit einer oder mehreren Gruppen, unabhängig ausgewählt aus der Gruppe, bestehend aus:

- C_{1-8}-Alkyl, lineares oder verzweigtes C_{1-8}-Alkenyl, C_{5-6}-Cycloalkyl,
- Phenyl wie in b) definiert,
- 5-6-gliedrige aromatische Ringgruppe mit einem oder mehreren Heteroatomen, ausgewählt aus N, S und O,
- Halogen,

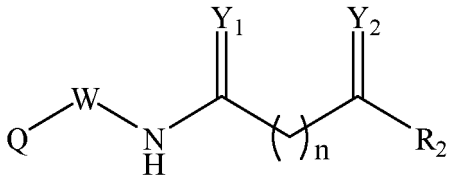
- (C_{1-6}-Alkyl)OCH_2-,
- C_{1-6}-Alkoxy,
- NR_aR_b, wobei R_a und R_b unabhängig voneinander aus C_{1-6}-Alkylgruppen oder Arylgruppen ausgewählt sind, und
- NHC(O)Rs-, -C(O)NH-Rs, -OC(O)Rs und -C(O)OR_5-, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, und

d) einem kondensierten bicyclischen Ring, der mindestens eine Phenylgruppe und eine aromatische heterocyclische C_{5-6}-Gruppe mit einem oder mehreren Heteroatomen, ausgewählt aus N, S und O, enthält, wobei die Phenylgruppe des kondensierten bicyclischen Rings gegebenenfalls substituiert ist mit einer oder mehreren Gruppen, unabhängig ausgewählt aus

- C_{1-8}-Alkyl, lineares oder verzweigtes C_{1-8}-Alkenyl, C_{5-6}-Cycloalkyl,
- Phenyl wie in b) definiert,
- 5-6-gliedrige aromatische Ringgruppe wie in c) definiert,
- Halogen,
- (C_{1-6}-Alkyl)OCH_2-,
- C_{1-6}-Alkoxy,
- OH, -SH oder -SR_5, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist,
- NR_6R_7, wobei R_6 und R_7 unabhängig voneinander ausgewählt sind aus C_{1-6}-Alkylgruppen, Arylgruppen, -C(O)Rs, -OC(O)Rs oder -C(O)ORs, wobei R5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, und
- NHC(O)Rs-, -C(O)NH-Rs, -OC(O)R_5, und -C(O)ORs-,wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist,

wobei der Begriff "Alkyl" zyklische Gruppen einschließt, und mit der Maßgabe, dass, wenn Y_1=Y_2=O; n= 0; R_2=$NHNH_2$ und W NH ist, Q keine Phenylgruppe ist, oder eine pharmazeutische Zusammensetzung, die diese Verbindung und einen pharmazeutisch annehmbaren Hilfsstoff zur Verwendung in der Medizin umfasst.

7. Pharmazeutische Zusammensetzung, umfassend eine Verbindung der Formel (II)



(II)

oder ein pharmazeutisch verträgliches Salz, Stereoisomer oder Solvat davon, wobei
Y_1= O;
Y_2= O;
W= NH
n= 0, 1;
R_2= NHR_4, und wobei R_4 ausgewählt ist aus OH, -NH_2, -NH-CH_3 und -NR_aR_b, wobei
R_a und R_b unabhängig voneinander ausgewählte C_{1-6}-Alkylgruppen oder Arylgruppen sind,
Q ausgewählt ist aus einer Gruppe bestehend aus:

a) 1-Pyridin, 2-Pyridin, 3-Pyridin,
b) Phenyl, gegebenenfalls substituiert mit einer oder mehreren Gruppen, unabhängig ausgewählt aus C_{1-8}-Alkyl, C_{2-8}-Alkenyl, Halogen, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, -OC(O)R_5, CF_3, CN, NH_2, -NHOH, -NH-NH_2, -NH-CH_3 und -NR_6R_7, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, wobei R_6 und R_7 unabhängig voneinander aus C_{1-6}-Alkylgruppen, Arylgruppen, -C(O)Rs, -OC(O)Rs oder -C(O)ORs-ausgewählt sind,
c) ein 5-6-gliedriger aromatischer Ring mit einem oder mehreren Heteroatomen, ausgewählt aus N, S und O, der gegebenenfalls mit einer oder mehreren Gruppen substituiert ist, die unabhängig voneinander ausgewählt sind aus:

- C_{1-8}-Alkyl, lineares oder verzweigtes C_{1-8}-Alkenyl, C_{5-6}-Cycloalkyl,

- Phenyl wie in b) definiert,
- 5-6-gliedrige aromatische Ringgruppe mit einem oder mehreren Heteroatomen, ausgewählt aus N, S und O,
- Halogen,
- (C_{1-6}-Alkyl)OCH_2-,
- C_{1-6}-Alkoxy,
- NR_aR_b, wobei R_a und R_b unabhängig voneinander aus C_{1-6}-Alkylgruppen oder Arylgruppen ausgewählt sind, und
- NHC(O)Rs-, -C(O)NH-Rs, -OC(O)Rs und -C(O)ORs-,wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, und

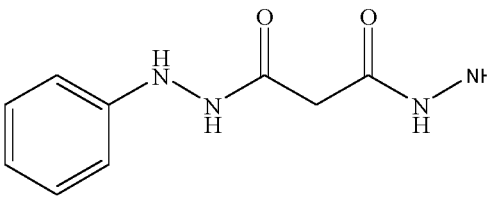
d) einem kondensierten bicyclischen Ring, der mindestens eine Phenylgruppe und eine aromatische heterocyclische C_{5-6}-Gruppe mit einem oder mehreren Heteroatomen, ausgewählt aus N, S und O, enthält, wobei die Phenylgruppe des kondensierten bicyclischen Rings gegebenenfalls mit einer oder mehreren Gruppen substituiert ist, unabhängig ausgewählt aus

- C_{1-8}-Alkyl, lineares oder verzweigtes C_{1-8}-Alkenyl, C_{5-6}-Cycloalkyl,
- Phenyl, wie in b) definiert,
- 5-6-gliedrige aromatische Ringgruppe wie in c) definiert,
- Halogen,
- (C_{1-6}-Alkyl)OCH_2-,
- C_{1-6}-Alkoxy,
- OH, -SH oder -SR_5, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist,
- NR_6R_7, wobei R_6 und R_7 unabhängig voneinander ausgewählt sind aus C_{1-6}-Alkylgruppen, Arylgruppen, C(O)Rs, -OC(O)Rs oder -C(O)ORs, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist, und
- NHC(O)Rs-, -C(O)NH-Rs, -OC(O)Rs oder -$C(O)OR_5$-, wobei R_5 C_{1-6}-Alkyl, Aryl oder Wasserstoff ist,

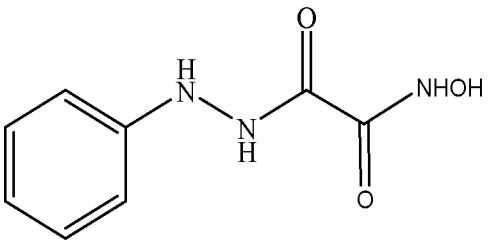
wobei der Begriff "Alkyl" zyklische Gruppen einschließt, und einen pharmazeutisch verträglichen Hilfsstoff zur Verwendung bei der Prävention und/oder Behandlung einer durch einen Pilz verursachten Infektion.

8. Pharmazeutische Zusammensetzung zur Verwendung nach einem der Ansprüche 6 oder 7, wobei Y_1=Y_2=O, n= 0 und Q eine Phenylgruppe ist, die gegebenenfalls in para-Position mit einer Gruppe substituiert ist, die aus der Gruppe ausgewählt ist, die aus H, Halogen, CH_3 und OCH_3 besteht.

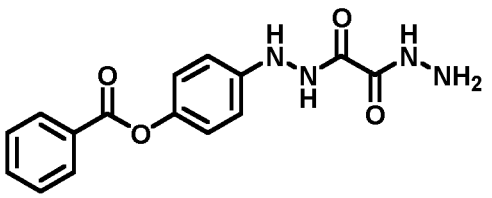
9. Pharmazeutische Zusammensetzung zur Verwendung gemäß Anspruch 7, wobei die Verbindung ausgewählt ist aus der Gruppe bestehend aus:



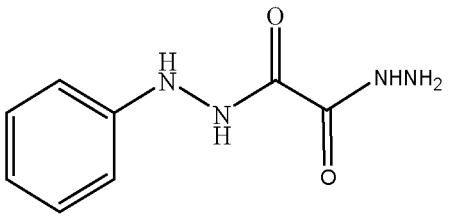
(Ia) MSG187



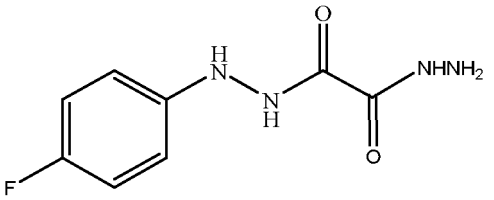
(Ib) MSG158



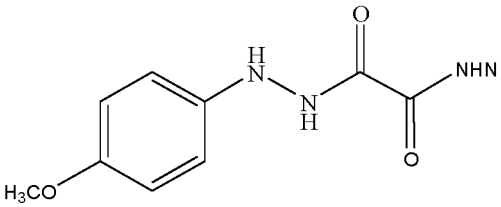
(Ig) MSG231



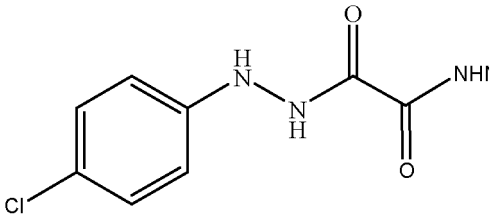
(IIa)MSG119



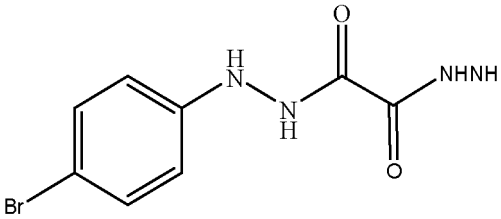
(IIb) MSG193



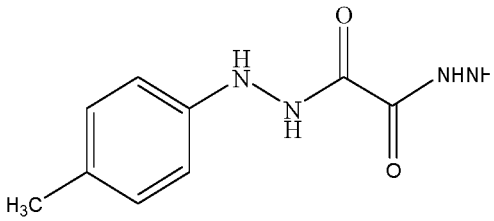
(IIc) MSG210



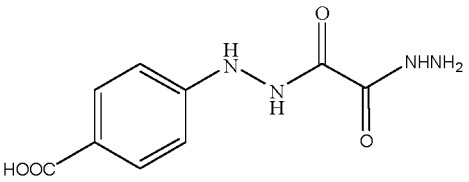
(IId) MSG214



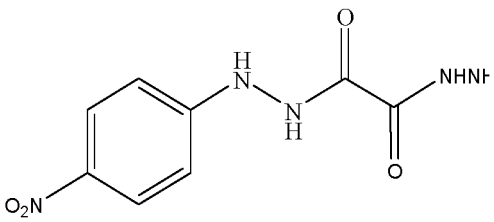
(IIe) MSG216



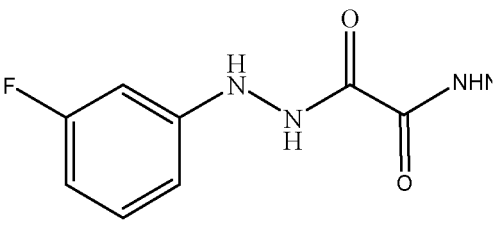
(IIf) MSG218



(IIg) MSG223

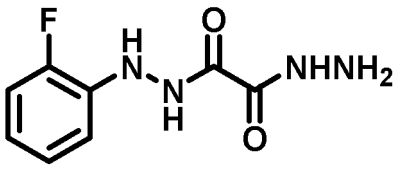


(IIh) MSG198



(IIi) MSG 227

und



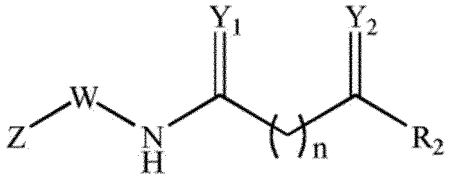
(IIj) MSG235

10. Pharmazeutische Zusammensetzung zur Verwendung nach einem der Ansprüche 7 bis 9, wobei der Pilz aus der Gattung *Candida, Aspergillus* oder *Saccharomyces* ausgewählt ist.

11. Pharmazeutische Zusammensetzung zur Verwendung nach Anspruch 10, wobei der Pilz aus der Gattung *Candida C. albicans, C. parapsilopsis, C. tropicalis, C. lusitaniae, C. guilliermondi* ist, der Pilz aus der Gattung *Aspergillus A. fumigatus, A. flavus, A. niger oder A. terreus* ist und/oder der Pilz aus *Saccharomyces S. cerevisiae* ist.

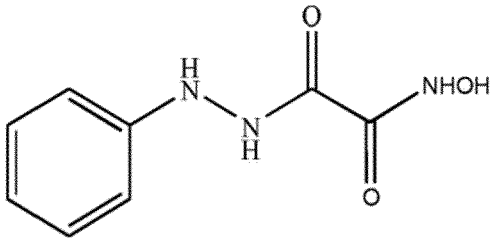
Revendications

1. Un composé de formule (1) :



(I)

ou un sel, stéréoisomère ou solvate pharmaceutiquement acceptable de celui-ci, dans lequel
Y_1 = O;
Y_2 = O ;
W=NH;
n = 0, 1 ;
R_2 = NHR_4, dans lequel R_4 est choisi dans le groupe constitué de OH, $-NH_2$, $-NH-CH_3$ et $-NR_aR_b$, dans lequel R_a et R_b sont des groupes alkyle en C_{1-6} ou des groupes aryle sélectionnés indépendamment ; Z = 1-pyridine, 2-pyridine, 3-pyridine ou phényle, le phényle étant optionnellement substitué par un ou plusieurs groupes indépendamment sélectionnés dans le groupe constitué d'alkyle en C_{1-8}, d'alcényle en C_{2-8}, d'halogène, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, NHOH, $-NH-NH_2$, $-NH-CH_3$ et $-NR_6R_7$, R_5 représentant un alkyle en C_{1-6}, un aryle ou l'hydrogène, R_6 et R_7 étant indépendamment choisis parmi un alkyle en C_{1-6}, un aryle, -C(O)Rs, -OC(O)Rs ou -C(O)ORs, le terme « alkyle » incluant des groupes cycliques, à condition que lorsque Yi = Y_2 = O ; n = 0 ; R_2 = $NHNH_2$ et W est NH alors Z n'est pas un groupe choisi dans le groupe constitué d'un groupe pyridine et d'un groupe phényle dans lequel le groupe phényle est optionnellement substitué par un groupe méthyle, l'halogène, le NO_2 ou l'OCH_3 et à condition que le composé ne soit pas

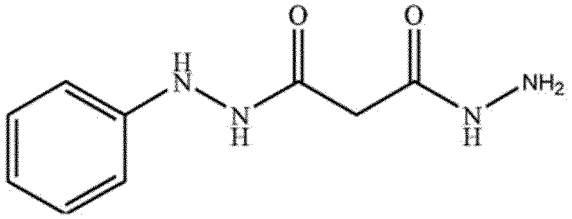


2. Le composé tel que défini à la revendication 1, dans lequel R_2 est NH-NH_2 et/ou dans lequel n vaut 1 et $Y_1 = Y_2 = O$.

3. Le composé tel que défini dans la revendication 1 ou la revendication 2, dans lequel Z est un groupe phényle optionnellement substitué par un ou plusieurs groupes indépendamment sélectionnés dans le groupe constitué d'un alkyle en C_{1-8}, alcényle en C_{2-8}, halogène, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, - OC(O)R_5, CF_3, CN, -NH_2, NHOH, -$NHNH_2$, -NH-CH_3 et -NR_6R_7, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène dans lequel R_6 et R_7 sont indépendamment choisis parmi des groupes alkyle en C_{1-6}, des groupes aryle, -C(O)Rs, -OC(O)Rs ou -C(O)OR_5.

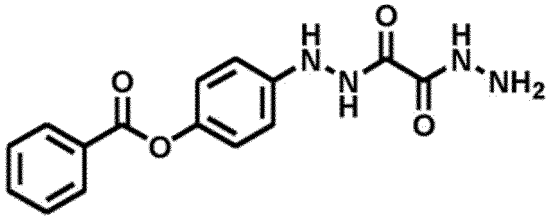
4. Le composé tel que défini dans la revendication 1, dans lequel R_4 est choisi dans le groupe constitué de -NH_2, -NH-CH_3 et -NR_aR_b, R_a et R_b étant des groupes alkyle en C_{1-6} ou des groupes aryle sélectionnés indépendamment.

5. Le composé tel que défini dans la revendication 1, ayant la formule suivante :



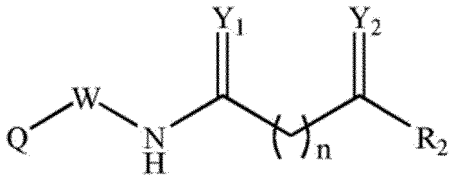
(Ia) MSG187

ou



(Ig) MSG231

6. Un composé de formule (II) :



(II)

ou un sel, stéréoisomère ou solvate pharmaceutiquement acceptable de celui-ci, dans lequel
$Y_1 = O$;
$Y_2 = O$;
W=NH;
n = 0, 1 ;
$R_2 = NHR_4$, R_4 étant choisi dans le groupe constitué de OH, -NH_2, -NH-CH_3 et - NR_aR_b, R_a et R_b étant des groupes alkyle en C_{1-6} ou des groupes aryle sélectionnés indépendamment ;
Q est sélectionné dans un groupe composé de :

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) un phényle optionnellement substitué par un ou plusieurs groupes indépendamment sélectionnés dans le groupe constitué de alkyle en C_{1-8}, alcényle en C_{2-8}, halogène, -SH, $-OR_5$, $-SR_5$, OH, NO_2, $C(O)NH-R_5$, $-C(O)OR_5$, $-OC(O)R_5$, CF_3, CN, $-NH_2$, -NHOH, $-NH-NH_2$, $-NH-CH_3$ et $-NR_6R_7$, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène, R_6 et R_7 étant sélectionnés indépendamment à partir de groupes alkyle en C_{1-6}, de groupes aryle, -C(O)Rs-, -OC(O)Rs ou -C(O)ORs,
c) un cycle aromatique à 5 ou 6 chaînons ayant un ou plusieurs hétéroatomes sélectionnés dans le groupe constitué de N, S et O et étant optionnellement substitué par un ou plusieurs groupes indépendamment sélectionnés dans le groupe constitué par :

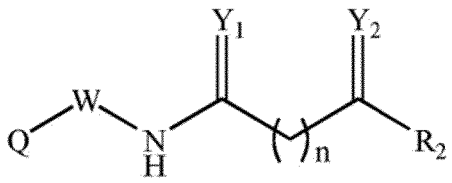
- un alkyle en C_{1-8}, alcényle en C_{1-8} linéaire ou ramifié, cycloalkyle en C_{5-6},
- un phényle tel que défini au point b),
- un groupe cyclique aromatique à 5 ou 6 chaînons ayant un ou plusieurs hétéroatomes sélectionnés parmi N, S et O,
- un halogène,
- $(C_{1-6}alkyl)OCH_2$-,
- alcoxy en C_{1-6},
- NR_aR_b, R_a et R_b étant indépendamment choisis parmi des groupes alkyle en C_{1-6} ou des groupes aryle, et
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$ et $-C(O)OR_5$-, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène, et

d) un cycle bicyclique condensé contenant au moins un groupe phényle et un groupe hétérocyclique aromatique en C_{5-6} ayant un ou plusieurs hétéroatomes sélectionnés parmi N, S et O, le groupe phényle dudit cycle bicyclique condensé étant facultativement substitué par un ou plusieurs groupes sélectionnés indépendamment parmi

- un alkyle en C_{1-8}, alcényle en C_{1-8} linéaire ou ramifié, cycloalkyle en C_{5-6},
- un phényle tel que défini au point b),
- un groupe cyclique aromatique à 5 ou 6 chaînons tel que défini au point c),
- un halogène,
- $(C_{1-6}alkyl)OCH_2$-,
- un alcoxy en C_{1-6},
- OH, -SH ou $-SR_5$ R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène,
- NR_6R_7, R_6 et R_7 étant indépendamment choisis parmi des groupes alkyle en C_{1-6}, des groupes aryle, -C(O)Rs, -OC(O)Rs ou -C(O)ORs, R_5 étant un alkyle en C_{1-6}, un aryle, ou l'hydrogène, et
- $NHC(O)R_5$-, $-C(O)NH-R_5$, $-OC(O)R_5$ et $-C(O)OR_5$-, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène,

le terme « alkyle » incluant des groupes cycliques et à condition que lorsque $Y_1 = Y_2 = O$; n = 0 ; $R_2 = NHNH_2$ et W est NH alors Q n'est pas un groupe phényle, ou une composition pharmaceutique comprenant ledit composé et un excipient pharmaceutiquement acceptable pour une utilisation en médecine.

7. Une composition pharmaceutique comprenant un composé de formule (II)



(II)

ou un sel, stéréoisomère ou solvate pharmaceutiquement acceptable de celui-ci, dans lequel
$Y_1 = O$;
$Y_2 = O$;
W = NH

n = 0, 1 ;
R_2 = NHR_4, et R_4 étant choisi parmi OH, -NH_2, -NH-CH_3 et -NR_aR_b, R_a et R_b étant des groupes alkyle en C_{1-6} ou des groupes aryle sélectionnés indépendamment,
Q est sélectionné dans un groupe constitué par :

a) 1-pyridine, 2-pyridine, 3-pyridine,
b) un phényle optionnellement substitué par un ou plusieurs groupes indépendamment sélectionnés parmi m alkyle en C_{1-8}, un alcényle en C_{2-8}, un halogène, -SH, -OR_5, -SR_5, OH, NO_2, C(O)NH-R_5, -C(O)OR_5, -OC(O)R_5, CF_3, CN, NH_2, -NHOH, -NH-NH_2, -NH-CH_3 ; et -NR_6R_7, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène, R_6 et R_7 étant des groupes alkyle en C_{1-6}, des groupes aryle, -C(O)Rs, -OC(O)Rs ou -C(O)ORs- sélectionnés indépendamment ;
c) un cycle aromatique à 5 ou 6 chaînons ayant un ou plusieurs hétéroatomes sélectionnés parmi N, S et O et étant optionnellement substitué par un ou plusieurs groupes indépendamment sélectionnés parmi :

- un alkyle en C_{1-8}, un alcényle en C_{1-8} linéaire ou ramifié, un cycloalkyle en C_{5-6},
- un phényle tel que défini au point b),
- un groupe cyclique aromatique à 5 ou 6 chaînons ayant un ou plusieurs hétéroatomes sélectionnés parmi N, S et O,
- un halogène,
- (C_{1-6}alkyl)OCH_2-,
- un alcoxy en C_{1-6},
- NR_aR_b, dans lequel R_a et R_b sont indépendamment choisis parmi les groupes alkyle en C_{1-6} ou les groupes aryle, et
- $NHC(O)R_5$-, -C(O)NH-R_5, -OC(O)R_5 et -C(O)OR_5-, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène, et

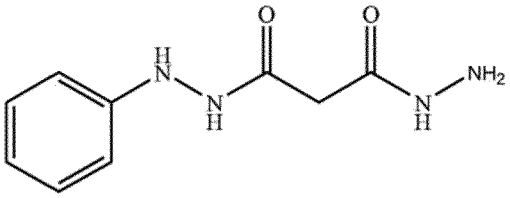
d) un cycle bicyclique condensé contenant au moins un groupe phényle et un groupe hétérocyclique aromatique en C_{5-6} ayant un ou plusieurs hétéroatomes sélectionnés parmi N, S et O, le groupe phényle dudit cycle bicyclique condensé étant facultativement substitué par un ou plusieurs groupes sélectionnés indépendamment parmi

- un alkyle en C_{1-8}, un alcényle en C_{1-8} linéaire ou ramifié, un cycloalkyle en C_{5-6},
- un phényle tel que défini au point b),
- un groupe cyclique aromatique à 5-6 chaînons tel que défini au point c),
- un halogène,
- (alkyle en C_{1-6})OCH_2-,
- C_{1-6}alcoxy,
- OH, SH ou -SR_5 R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène,
- NR_6R_7, dans lequel R_6 et R_7 sont indépendamment choisis parmi des groupes alkyle en C_{1-6}, des groupes aryle, C(O)Rs, -OC(O)Rs ou -C(O)ORs, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène, et
- $NHC(O)R_5$-, -C(O)NH-R_5, -OC(O)R_5 ou -C(O)OR_5-, R_5 étant un alkyle en C_{1-6}, un aryle ou l'hydrogène,

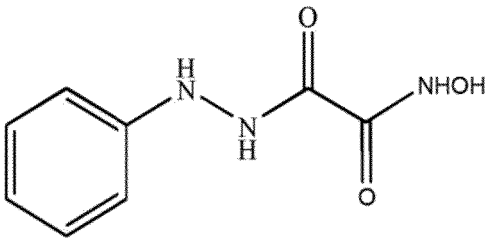
le terme « alkyle » incluant des groupes cycliques, et un excipient pharmaceutiquement acceptable destiné à être utilisé dans la prévention et/ou le traitement d'une infection provoquée par un champignon.

8. La composition pharmaceutique à utiliser selon l'une quelconque des revendications 6 ou 7, dans laquelle Y_1 = Y_2 = O, n = 0 et Q est un groupe phényle optionnellement substitué en position para par un groupe choisi dans le groupe constitué de H, halogène, CH_3 et OCH_3.

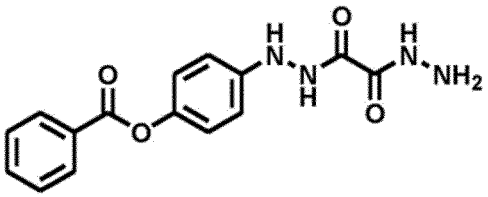
9. La composition pharmaceutique à utiliser selon la revendication 7, dans laquelle le composé est choisi dans le groupe constitué par :



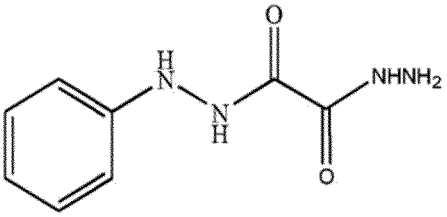
(Ia) MSG187



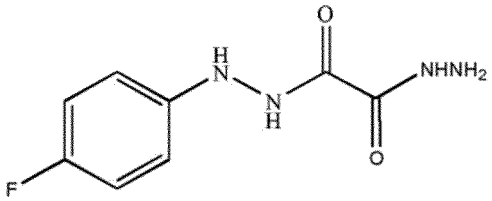
(Ib) MSG158



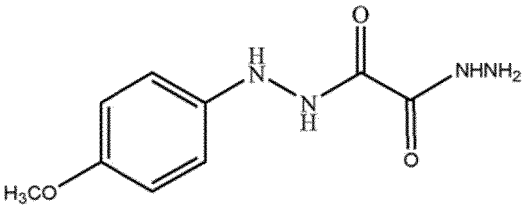
(Ig) MSG231



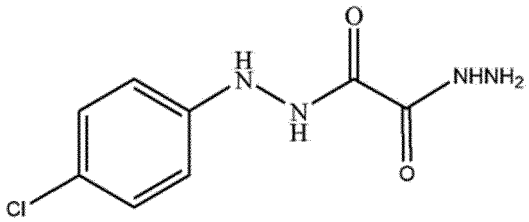
(IIa) MSG119



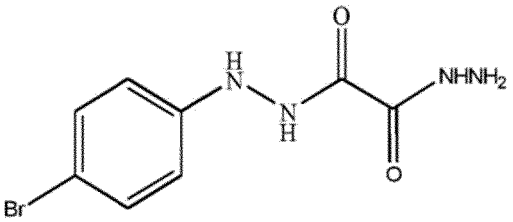
(IIb) MSG193



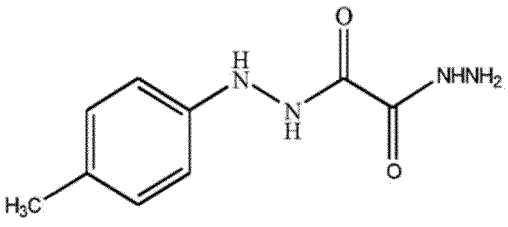
(IIc) MSG210



(IId) MSG214



(IIe) MSG216



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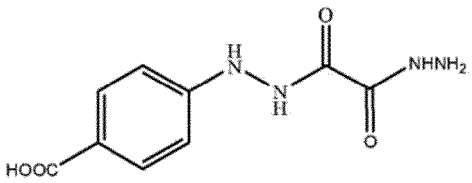
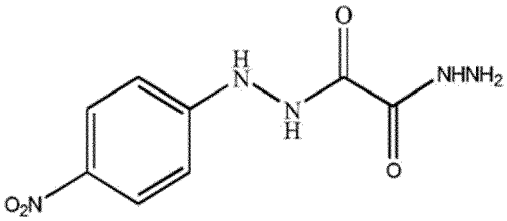


(IIf) MSG218 (IIg) MSG223



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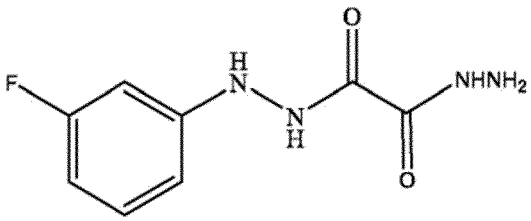
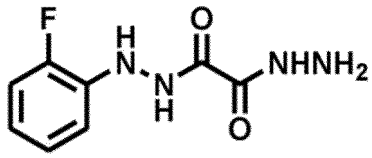


,

(IIh) MSG198 (IIi) MSG 227

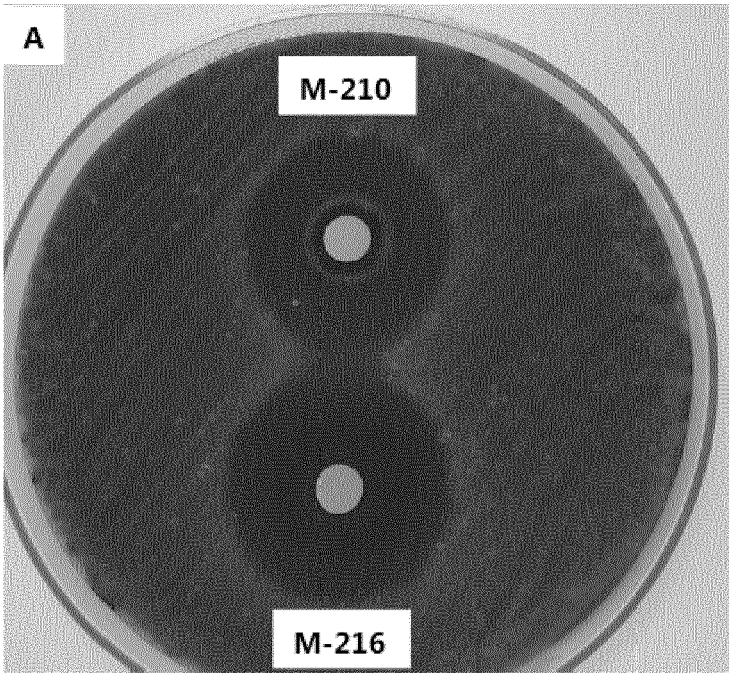
et



(IIj) MSG235

10. La composition pharmaceutique à utiliser selon l'une quelconque des revendications 7 à 9, dans laquelle le champignon est choisi parmi le genre *Candida, Aspergillus* ou *Saccharomyces.*

11. La composition pharmaceutique à utiliser selon la revendication 10, dans laquelle le champignon du genre *Candida* est C. *Albicans, C. parapsilopsis, C. tropicalis, C. lusitaniae, C. guilliermondi,* le champignon du genre *Aspergillus* est *A. fumigatus, A. flavus, A. niger* ou *A. terreus* et/ou le champignon de *Saccharomyces* est S. *cerevisiae*.



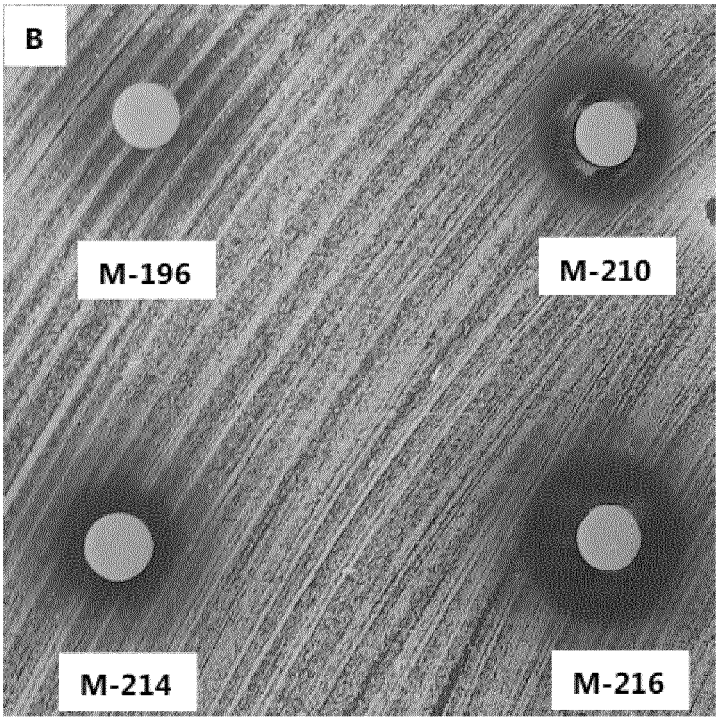


Fig. 1

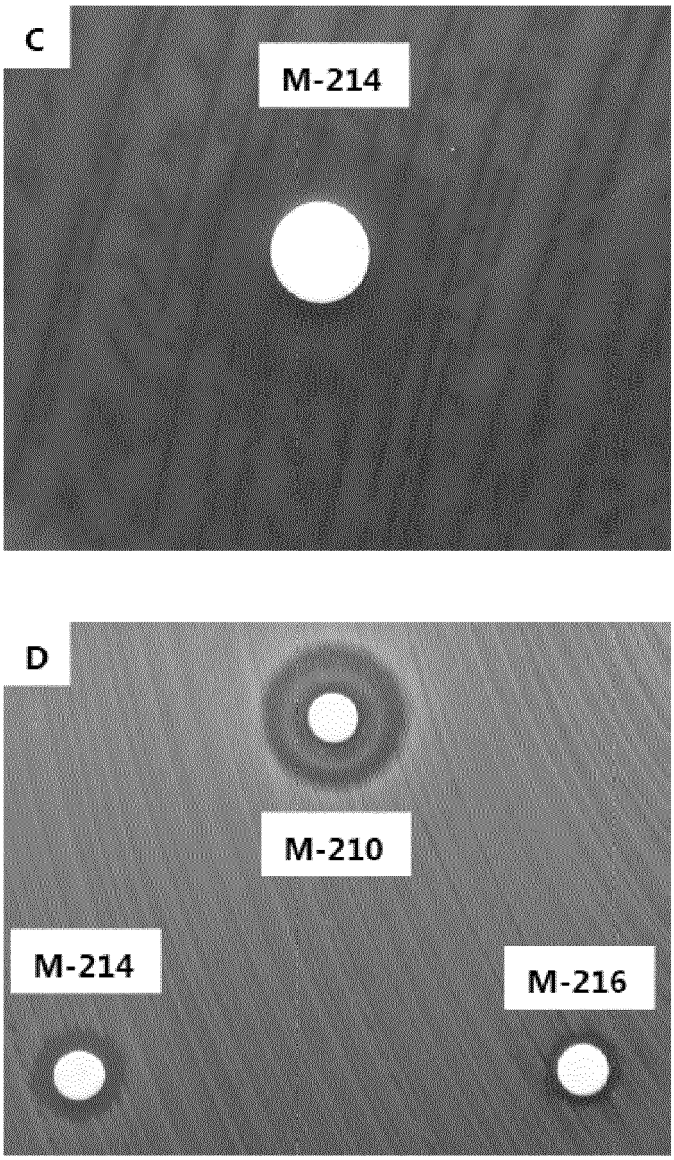
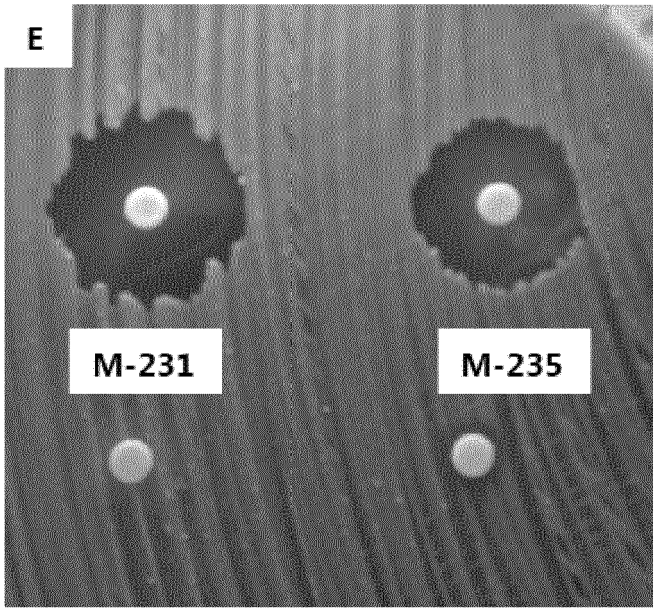


Fig. 1 (Cont.)



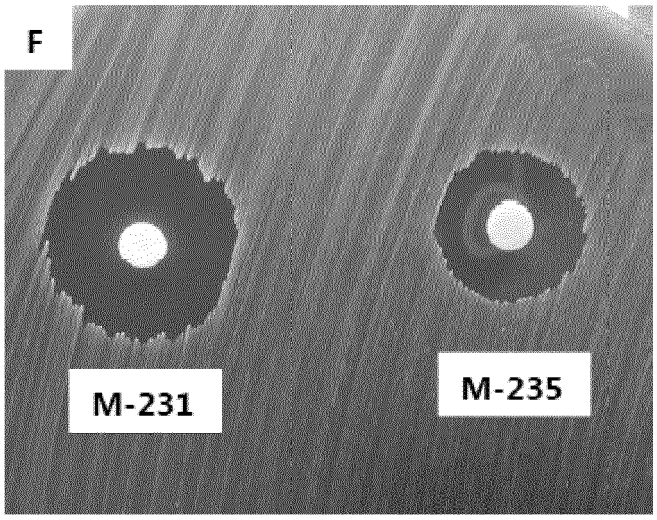


Fig. 1 (Cont.)

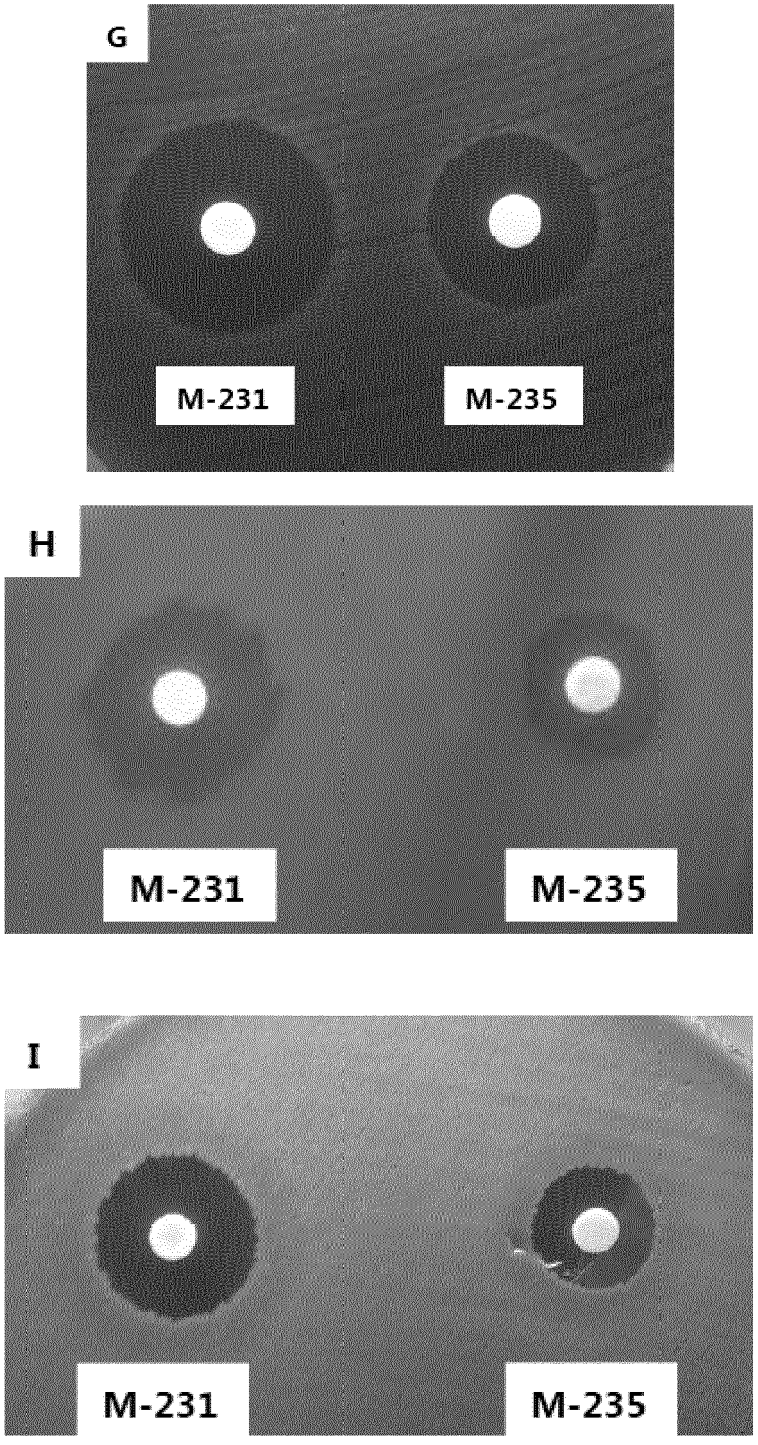


Fig.1 (Cont.)

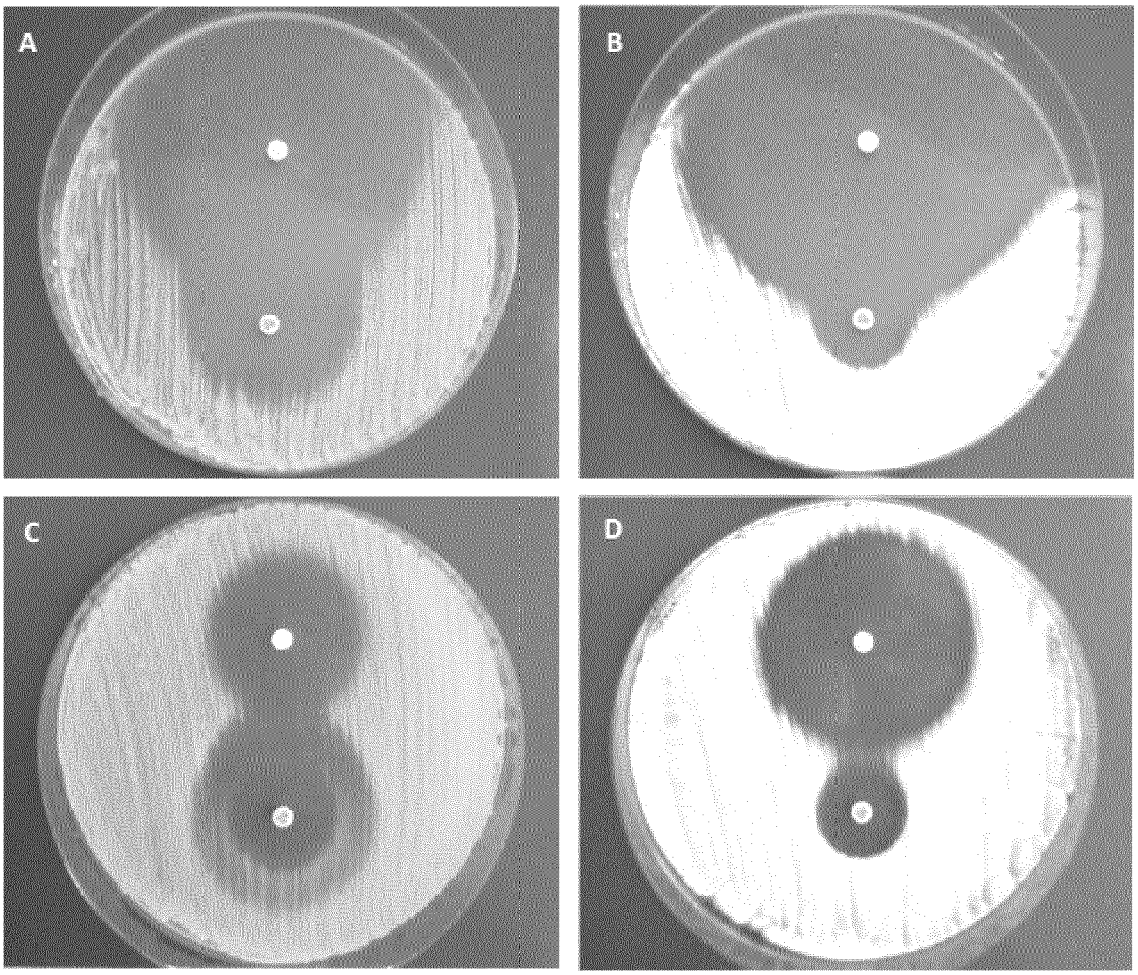


Fig. 2

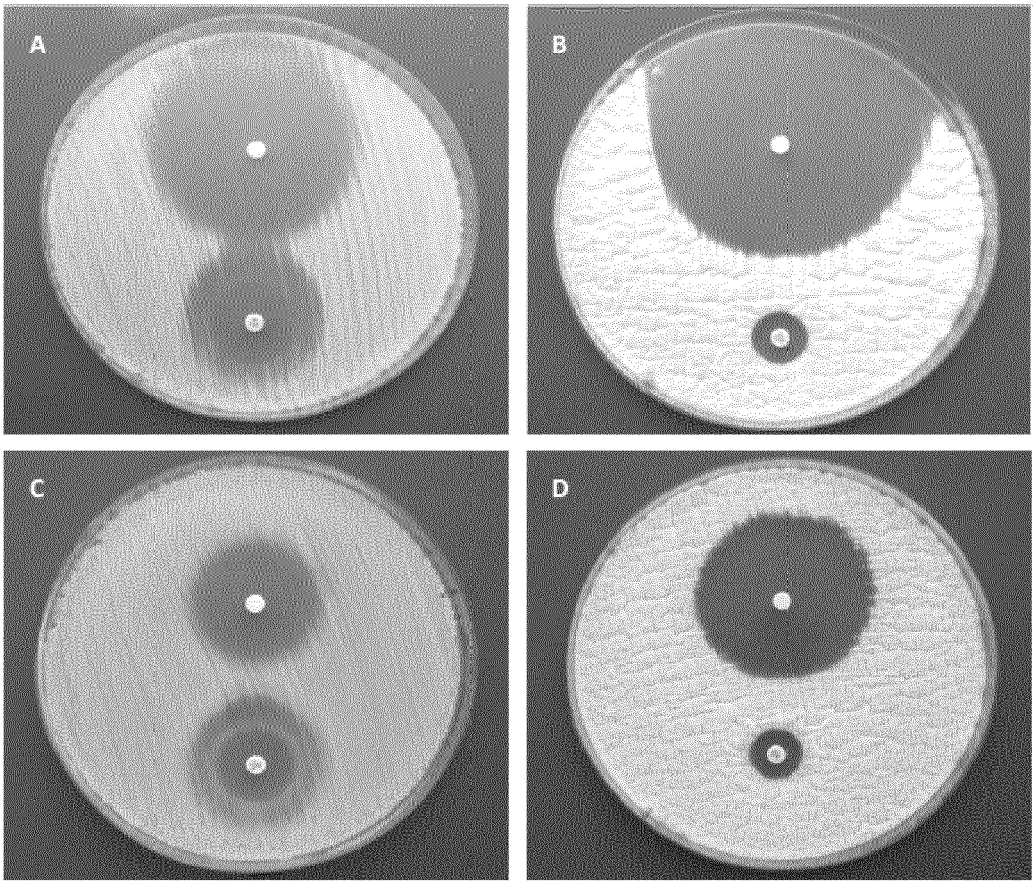


Fig.3

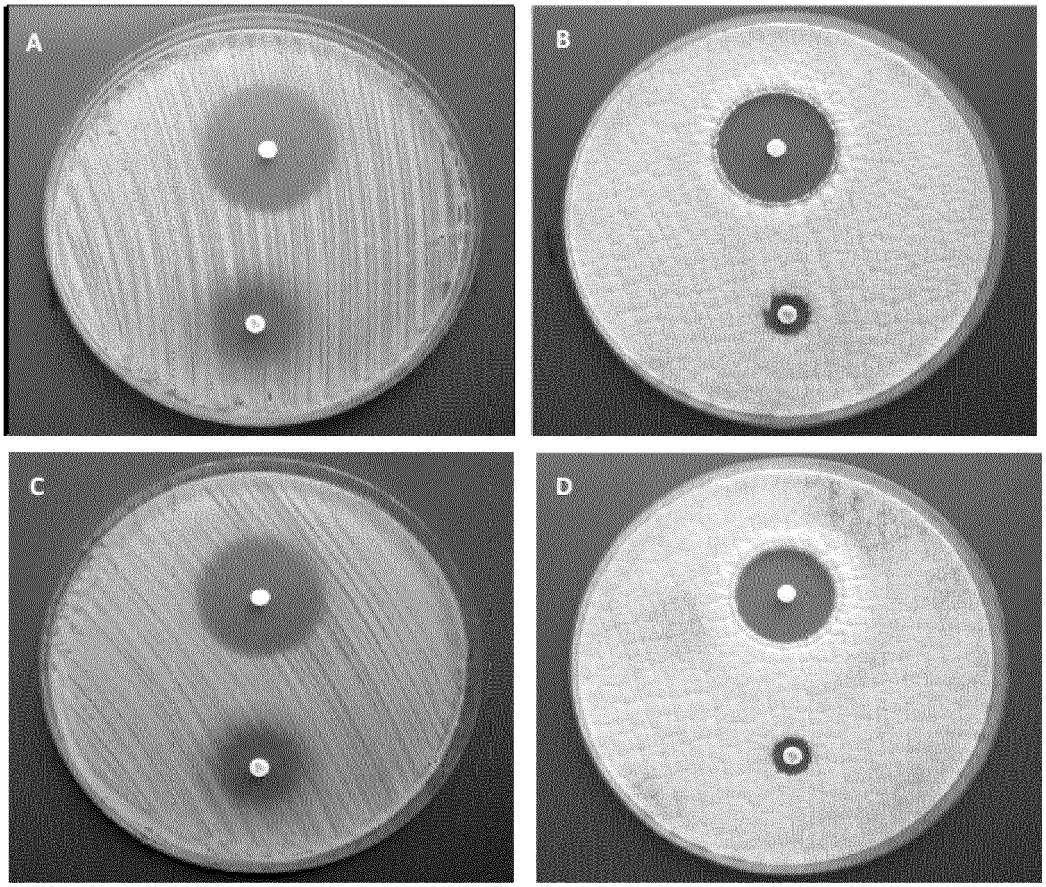


Fig. 4

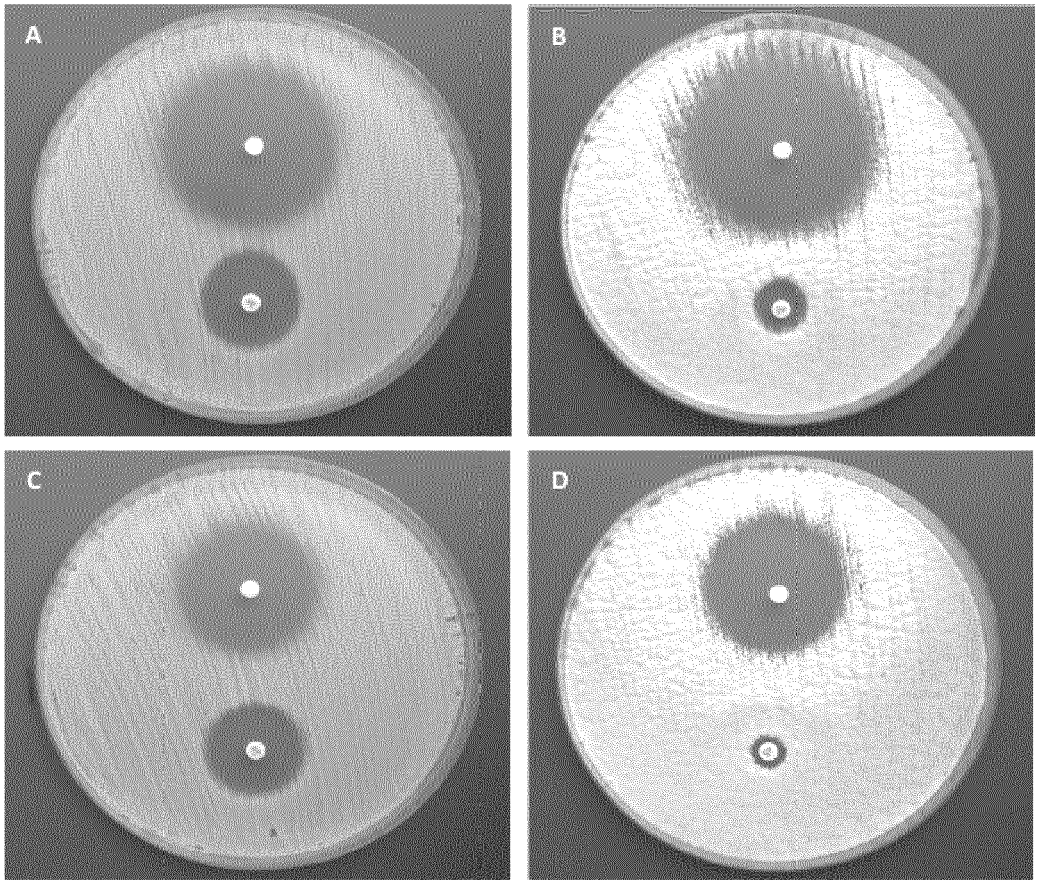


Fig. 5

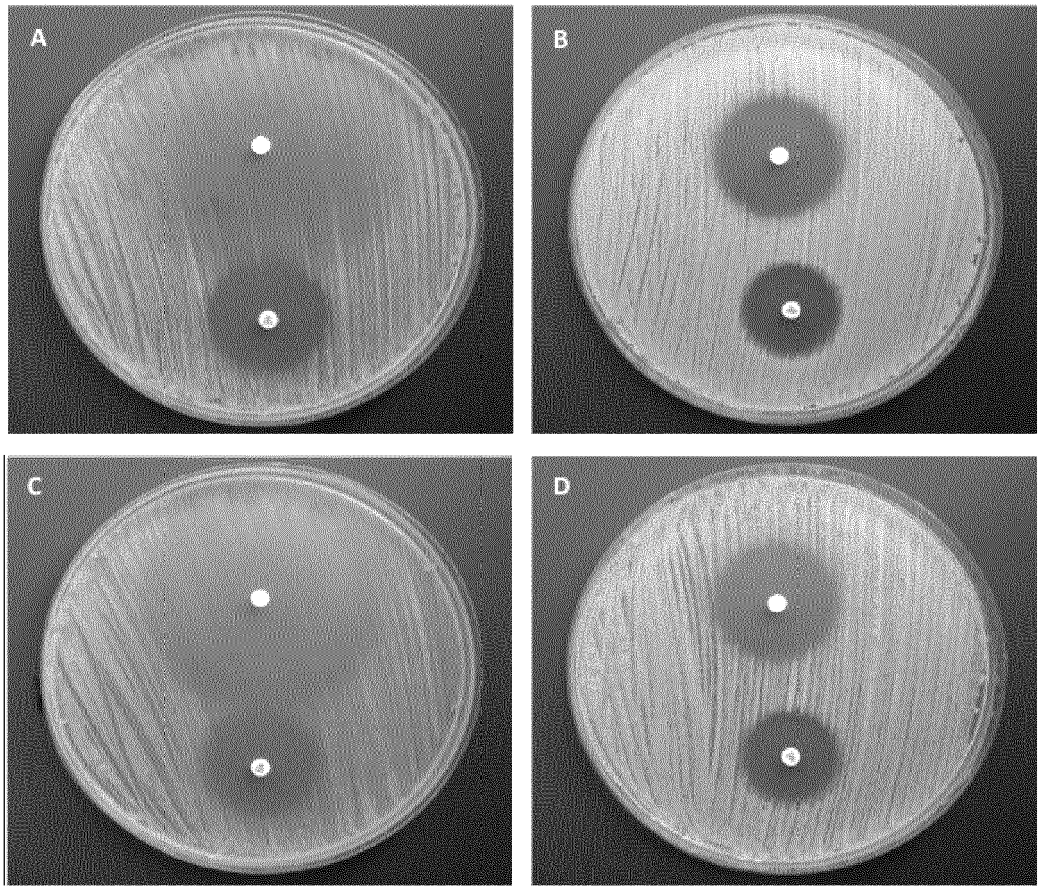


Fig. 6

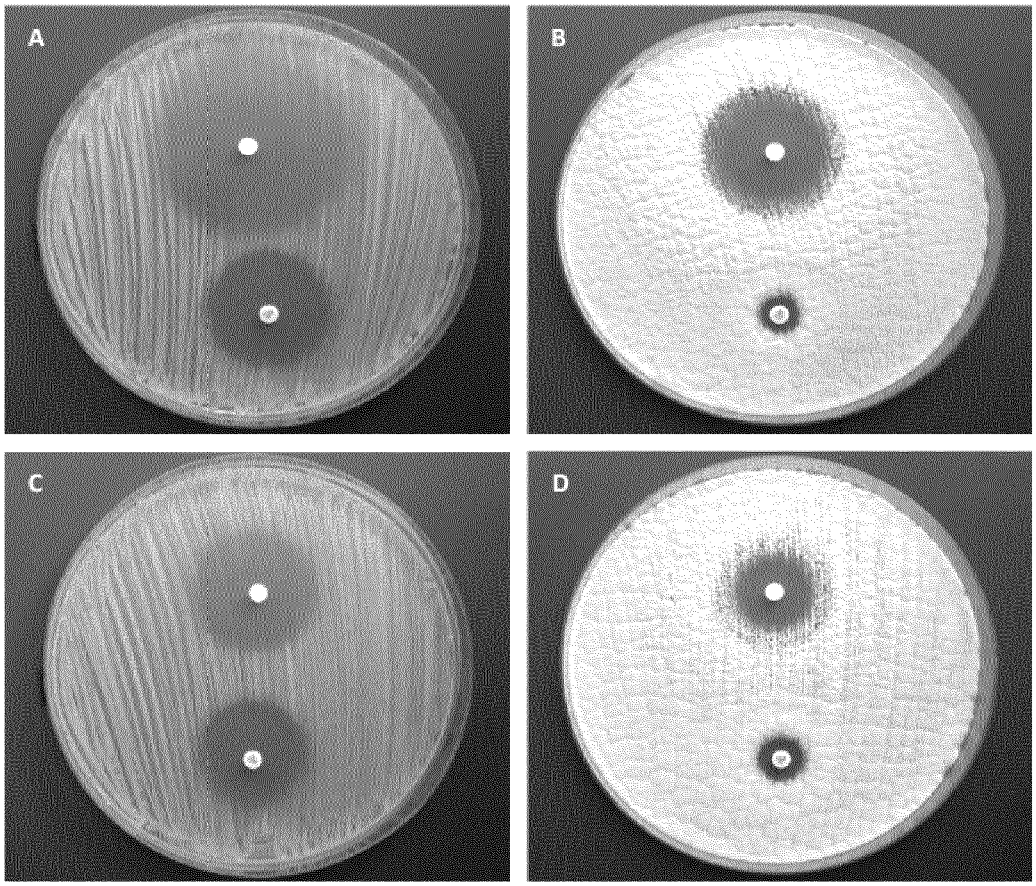


Fig. 7

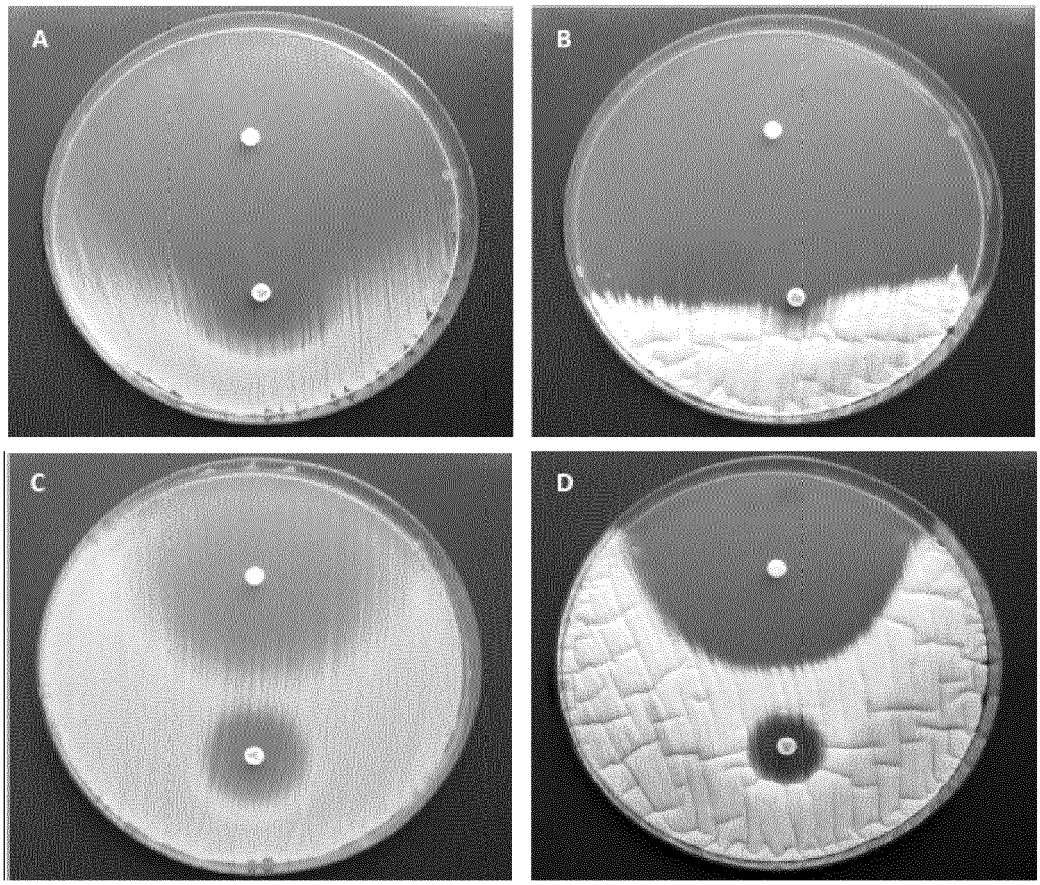


Fig. 8

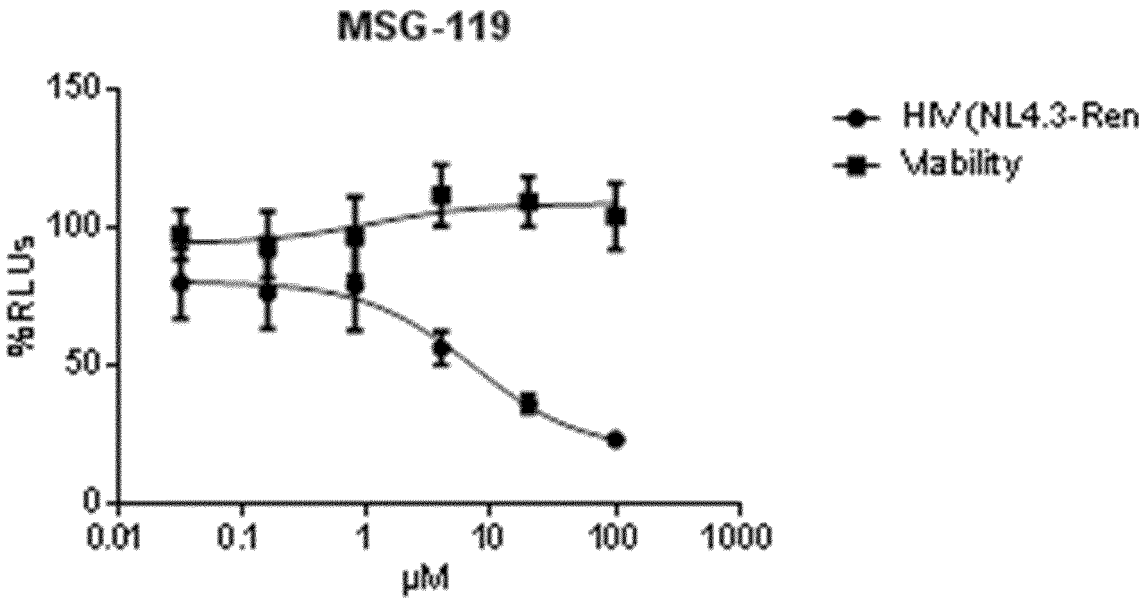

MSG-119
150
100
50
0
%RLUs
0.01
0.1
1
10
100
1000
μM
HIV(NL4.3-Ren
Viability

Fig. 9

REFERENCES CITED IN THE DESCRIPTION

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